TRANSACTIONS

OF

The Association of Life Insurance Medical Directors of America

SIXTY-FIRST ANNUAL MEETING

James R. Gudger, M. D.
Editor

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CONTENTS OF VOLUME XXXVI

Page

Officers, Executive Council, and Former Officers iv

Opening Remarks by Linford H. Lee, M. D. i

Welcoming Address by Lewis A. Alesen, M. D. 1

Papers:

Problems in Borderline Cardiovascular Disease States 5
George C. Griffith, M. D.

The Present Status of the Problem of Lipid Metabolic Disturbances and Their Relationship to the Genesis of Arterial Disease 13
John W. Gofman, M. D.

The Nature and Treatment of the Auricular Arrhythmias 27
Myron Prinzmetal, M. D.

Prolonged P–R Interval in Apparently Healthy People 44
Francis A. L. Mathewson, M. D.

The Business of Insurance and the Profession of Medicine 76
Ralph M. Filson, M. D.

Syncope, Vertigo, and Dizziness 90
Robert H. Williams, M. D.

Trauma and Heart Disease 100
Alan R. Moritz, M. D.

Greetings from Medical Section, American Life Convention 105
David S. Garner, M. D., Chairman

Prognosis in Latent Syphilis 107
Charles W. Barnett, M. D.

Coccidioidomycosis 121
William A. Winn, M. D.

The Muscular Atrophies 133
John B. Doyle, M. D.

Observations of a Medical Referee 144
John W. Wear, M. D.

Remarks by President-Elect Earl C. Bonnett 154

List of Those in Attendance 156

Obituary 158

List of Members of the Association 159

Honorary Members 178

Emeritus Members 178

Companies and Their Representatives 179

Index, Volume XXXVI 197

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Transactions of The Association of Life Insurance Medical Directors of America

SIXTY-FIRST ANNUAL MEETING

The Sixty-first Annual Meeting of The Association of Life Insurance Medical Directors of America was held at the Ambassador Hotel in Los Angeles, California, on Tuesday, Wednesday, and Thursday, October 21, 22, and 23, 1952.

PRESIDENT LEE — Gentlemen, this is a very distinct honor for me, and a rare pleasure, to open this sixty-first annual meeting of our organization.

Now, in some organizations, and previously in ours, it has been customary for the president to make a forty-five minute speech of welcome, but I am sure if I were to do so I would dwell upon climate rather than science.

I am greatly pleased to be able, however, to bring to you the president of our California state medical association who will welcome you to our state, our city, and our medical circles here. Dr. Lewis Alesen has been a long-time friend, and I am more pleased than I can tell you to present to you this morning a man who has contributed very greatly to the affairs of organized medicine, on the west coast particularly. Dr. Alesen.

DR. ALESEN — Mr. President, Ladies and Gentlemen — and in addressing you, Mr. President, I take cognizance of the fact that you and I have been good friends for many years:

When the historians get around to writing the history of our era, I believe they will characterize it as the flight from responsibility, and I should like to talk on that subject for just a few moments, because in my mind you gentlemen represent one of the most important "mechanisms" mankind has ever developed in

preparing and protecting himself against the many vicissitudes of economic and social life.

When the young man goes before the personnel director of any large corporation today, he does not ask what are the opportunities for advancement. He is interested in how much social security there is in the job — how much vacation with pay.

Now is that not a sad commentary upon your country and mine. Yet that represents a denial on the part of the individual of responsibility for his own welfare. You and I as doctors of medicine, having been trained in pathology, want to look to the cause of this peculiar mental attitude which results in a flight from responsibility, and we do not have to look too far.

Our progressive education under John Dewey, beginning in Columbia University back in 1910, began to express the importance of group action and to teach the current crop of voters — perhaps you and me to a limited extent, but certainly our sons and daughters — to reject and deny responsibility for themselves and to transfer that responsibility to the group. And, of course naturally, these individuals who are voting today look to big government. They are prepared for all manner of price and wage controls, for agricultural subsidies, for crop allocations, for federal housing.

These historians, when they continue their chronicle, will point out to future generations as they have done today that those societies in which the fundamental principle of individual responsibility has been recognized had, in fact, been the ones in which there had been the greatest variety of goods and services available to everyone within the societies. And when that principle has been violated by some type of collective action, of course we have had economic and social decay.

I should like to address a few remarks to the profession of science, the "mechanism" of insurance for which I have the deepest respect. You gentlemen have combined the operation of biologic law with the operation of the mathematical law of large numbers and you have come up with an excellent social "mechanism" for the protection of all.

I would like to point out to you that because you assess a certain specified premium in return for a specified benefit, you are indeed

acting in accordance with national law which states that the reward shall be very definitely in terms of the merit, that is, the amount of contribution made. And the penalty, of course, depends on whether the man forfeits his policy by failure to pay the premium — he is penalized directly for that failure. Nowhere in your "mechanism" is there this group concept: "From each according to his ability; to each according to his need."

That is why insurance has been successful. That is why the greedy collectivists are eyeing your reserves. That is why most of the states collect a high premium tax, and why the federal government from time to time looks into your operations and hopes to change them. The fundamental purpose of the collectivists — and I mean any of these philosophies, Marxism, Socialism, Fascism, Communism, New Dealism, for they are all fundamentally the same — is that they insist the individual deny responsiblity for himself and place that responsibility upon the State. The fundamental purpose is to see that a successful private venture fails in order that government may rush into the vacuum so created.

Hard words, Mr. President, yet they are borne out by the hard facts of history. And so I think insurance has a wonderful opportunity.

I have wondered, and I have asked some of my friends in the insurance business, just why it is that the insurance business does not take advantage of their long lists of premium-paying individuals and inform them as to just what is happening to our economic and social structure; inform them that the dollar paid out in premiums for the past 20 years has gradually deteriorated and degenerated so that the face value of the policy, while of course it will be returned in a like number of dollars, has lost the purchasing power by at least fifty per cent.

We have not done a bad job on the health of the American people. I am sick and tired of the detractors who would tell our people that the American people cannot possibly get good medical care because they cannot afford it.

Just a figure or two will serve to refute that peculiar argument. In the year 1950, and I am quoting figures now from the Bureau of Medical Economic Research, the American people spent eight billion dollars for medical care. That was four and two-tenths

per cent of their total expenditure for personal services and goods of about one hundred ninety-three billion, six million dollars. That same year they spent five and six-tenths per cent for recreation and two and three-tenths per cent for tobacco. They spent three times as much for alcohol, tobacco, and recreation as for medical care; and yet it is alleged that the American people cannot afford good medical care. That is merely a political subterfuge.

We know that we, in medicine, have done an excellent job in making available to the people of this country fine structures such as Blue Cross, Blue Shield, for the prepayment of the cost of illness. Let us not apologize for American medicine. Let us continue in the same general direction.

PRESIDENT LEE — Thank you very much, Dr. Alesen. Unfortunately, Dr. Alesen has to go over to the operating room and cannot stay with us but he promised to join in some of our social activities if time will permit, and we are very grateful to him.

Now I shall introduce another good friend, Dr. George C. Griffith, Professor of Medicine, School of Medicine of the University of Southern California, a friend of the medical student and doctor, and a most gracious consultant. His subject is "Problems in Borderline Cardiovascular Disease States." Dr. Griffith.

PROBLEMS IN BORDERLINE CARDIOVASCULAR DISEASE STATES

GEORGE C. GRIFFITH, M. D.

Professor of Medicine, Coordinator of Cardiovascular Diseases
University of Southern California School of Medicine
Los Angeles, California

Galen and his fellow physicians had no knowledge of heart disease; they attributed observed variations in pulse to the emotions and to environmental stimuli. Such was the practice until the sixteenth century, when the researches of Vesalius and Harvey amassed evidence of the frequency and chronicity of heart disease. From this time, attempts were made to correlate disease states with heart lesions until, at the opening of the nineteenth century, this practice was so widespread that Corvisart and Virchow imputed almost all observed illness to cardiovascular disease. In 1836, however, an Edinburgh physician, John Calthrop Williams, published an important volume which differentiated between "functional" and "organic" derangements of the heart and laid the groundwork for more careful nosologic investigation.

At the present time, we recognize many factors which exert a transient influence on heart size and/or heart action. Therefore, we hesitate to make a diagnosis of organic heart disease unless *several* objective signs or symptoms of cardiovascular disease are present in the patient, which signs — by complementing and reinforcing one another — create an unmistakable disease pattern. Among such objective manifestations of disease are included: 1) the presence of an etiologic factor or factors capable of producing heart disease; 2) pronounced alteration in heart size and contour; 3) significant alterations of heart sounds; 4) abnormal cardiac pulsations; 5) important alterations in the electrocardiographic pattern; 6) significant disturbances of cardiac rhythm; and 7) evidences of cardiac decompensation.

Appraisal of heart size

Cardiac enlargement is commonly accepted as indicative of the presence of a disease process, the degree of enlargement reflecting

in a measure the degree to which the normal physiologic action of the heart is disturbed. Thus, one of the first problems of the physician in his appraisal of cardiac status in the patient is to determine whether or not cardiac enlargement or characteristic alterations of the cardiac contour are present.

Heart size, however, is dependent upon many factors: age, sex, weight, size — even time of day. From an average of 20 to 25 Gm. at birth, heart weight increases to approximately 100 Gm. in the eight-year-old, 200 Gm. in the teen age youngster, and between 200 and 350 Gm. in the adult. The heart of the male is somewhat heavier than that of the female, averaging 300 Gm. in the adult male as compared with 250 Gm. in the adult female.

Body weight is also of account, the heart of the obese patient weighing more than the heart of a spare individual of the same age and sex. In fact, heart weight of the normal individual may be expressed as a definite percentage of body weight. In interpreting the cardiac silhouette of the obese individual, the clinician must be wary of the epicardial pad of fat that is often present and must remember that the high position of the diaphragm will make the heart appear larger than it actually is.

The occupation of the patient may be important, as cardiac muscle may show some hypertrophy in persons engaged in strenuous occupations or who pursue vigorous sports (such as that of under-water swimmer), even in the absence of cardiac pathology.

Body build of the patient may give false clues as to the size of the heart: for example, the hearts of children appear relatively larger than those of adults.

Displacement of the heart

The height of the diaphragm is most important in the analysis of x-ray films and electrocardiograms. The enlarging abdomen with ascites or fat will raise the diaphragm, making the heart appear larger. On the other hand, the deep lowering of the diaphragm in emphysema will make the patient's heart appear smaller than it actually is. Less important but noteworthy are the movements of the diaphragm during ordinary breathing and in the presence of certain intra-abdominal diseases.

Trained clinical judgment is necessary to determine whether

the presence of marked depression of the sternum (the so-called funnel chest) has in the particular instance merely resulted in a displacement of the heart without an attendant handicap or is seriously embarrassing heart action in the patient. The problem is somewhat similar in assessing the increased load placed upon the right ventricle or left ventricle or both, in scoliosis.

Infrequently, cases of congenital dextrocardia of the "mirror type" are observed, in which the "left" chambers of the heart lie on the right side, and the "right" chambers on the left side. Dextrocardia of this type is of little clinical importance unless associated with other cardiovascular defects.

Physiologic measurements; the appraisal of cardiac function

Among methods for appraisal of cardiac sufficiency are included: electrocardiographic measures and measures of heart rate, blood pressure, venous pressure, circulation times and stroke volume. In addition, cardiac catheterization procedures have recently made possible measurement of pulmonary arterial pressure and the study of the right chambers of the heart.

In evaluating the heart action of the individual patient, the clinician must bear in mind the many factors that are reflected in cardiac function. For example, nervous tension can cause the pulse to race, or an iced drink can produce a temporary inversion of the T waves in the electrocardiogram. The state of health of the patient at the time of examination is most important: severe infectious states, anemia, thyrotoxicosis, and many other diseases can temporarily alter cardiac findings in the absence of any cardiac pathology.

Growing children are very prone to show instability of circulation or heart action; illness or infection may sometimes cause a temporary systolic murmur in the heart of a child who is growing rapidly. Altitude, temperature, occupation, drugs, emotions — all of these affect heart function and are, in turn, reflected in physiologic measurements of heart action.

Arrhythmias

BRADYCARDIA is a normal mechanism in some individuals. In others, it occurs as a reaction to certain diseases or drugs.

Bradycardia is seldom of organic origin except when due to the presence of atrioventricular block.

TACHYCARDIA, too, rarely is a reaction to heart disease. Tachycardia may result from apprehension, excitement or pain. It may be a reaction to sympathetic nerve stimulation by drugs such as epinephrine or substances such as tea, coffee or tobacco. Again, tachycardia may indicate the presence of toxins, of infection or of pulmonary embolism.

PREMATURE HEART CONTRACTIONS (extrasystoles) are common in normal adult hearts, although they are rarely observed in the heart of the infant or child. Although relatively more numerous in hearts with structural abnormalities than in "normal" hearts, premature contractions do not in themselves bespeak the presence of cardiac disease. They are of diagnostic significance in two instances: 1) After myocardial infarction, they frequently presage the onset of ventricular tachycardia or ventricular fibrillation. 2) During digitalization or anesthesia, they indicate toxic poisoning.

PAROXYSMAL TACHYCARDIA is unimportant in the absence of associated cardiac findings; most cases of this disturbance occur in apparently normal hearts. However, structural changes such as mitral stenosis or cardiac infarction favor the occurrence of paroxysmal tachycardia, and thyrotoxicosis is often accompanied by either atrial paroxysmal tachycardia or paroxysmal atrial fibrillation.

PAROXYSMAL AURICULAR FLUTTER and FIBRILLATION rarely occur in the normal heart; however, in cases where they are not accompanied by other cardiac pathology, life expectancy is unchanged by their presence.

Heart sounds and murmurs

Heart sounds are increased in intensity after exercise or excitement, or if the wall of the chest is thin. They are muffled somewhat in emphysema, during weakness or shock, or if the chest wall is unusually thick. Third sounds are often heard in the hearts of healthy young individuals, occurring after the second heart sound. They have no clinical significance. A midsystolic click is sometimes heard which has been attributed incorrectly to heart disease.

Most systolic murmurs do not indicate the presence of organic heart disease. Some of these murmurs have little significance; others indicate the presence of diseases outside the cardiovascular system that act upon the cardiac mechanism. The safest course to pursue is to investigate all murmurs except pulmonary systolic murmurs to determine, if possible, the cause. Unless a pulmonary systolic murmur is of considerable intensity when the patient is in an upright position, it may usually be disregarded as physiologic. Aortic and apical systolic murmurs, too, are for the most part physiologic unless associated with selective chamber enlargement.

A venous hum in the neck is frequently found in normal individuals, especially in children, and has no pathologic significance. However, diagnostic errors are sometimes occasioned by the fact that the hum may be transmitted downward over the base of the heart or close to the lower end of the sternum, where it may be confused with pathologic heart murmurs. If the patient is placed in the Trendelenburg position, the venous hum originating in the neck will disappear.

The continuous murmur of a pulmonary arteriovenous fistula is sometimes confused with patency of the ductus arteriosus or even with mitral disease. The differentiation of these conditions is imperative because they now can be corrected surgically.

The apical filling diastolic murmur of hypervolemia (as in pregnancy or hypermetabolism) is frequently confused with mitral stenosis. Absence of selective left atrial enlargement confirms the physiologic character of the apical filling diastolic murmur.

Abnormalities of breathing

At times even the experienced clinician has difficulty in determining whether dyspnea observed in a particular patient is of cardiac or pulmonary origin. Subjectively, the symptoms are identical. Cough, hemoptysis or cyanosis may accompany dyspnea of either cardiac or pulmonary origin. In early phases of congestive heart failure, the physician must search for collateral evidence to establish his diagnosis. In dyspnea of cardiac origin, circulation time is slowed, venous pressure levels are increased, and the administration of a mercurial diuretic results in an increased output of urine.

Contrary to popular belief, sighing respiration, rapid breathing, or slow breathing does not indicate the presence of heart disease. However, when periods of hyperpnea alternate periodically with periods of apnea (the so-called Cheyne-Stokes respiration), left ventricular weakness and poor supply of blood to the respiratory center are usually present. Slight degrees of periodic apnea and hyperpnea may exist, nevertheless, without the presence of heart disease.

Precordial pain

Precordial pain due to cardiac insufficiency must be distinguished from the discomforts which sometimes accompany exertion in normal persons, from pains which may accompany nervousness or indigestion, and from pains which indicate the presence of esophageal lesions, a hiatus hernia, arthritic conditions, or the "short leg syndrome." (In the "short leg syndrome," the disproportionate length of the legs places a strain on the muscles of the spine. The pain associated with this muscle strain is often referred to the chest region.)

Other non-cardiac conditions

Several conditions which are at times erroneously attributed to cardiac pathology because of the faintness, giddiness and dizziness involved are the carotid sinus syndrome (due to overactivity of the sinus reflex), the hyperventilation syndrome, symptoms arising from cerebral arteriosclerosis or cerebral thrombosis, and Meniere's syndrome. Meniere's syndrome can be differentiated from heart disease by the presence of vertigo.

COMMENT

In borderline cases, the decision as to whether or not cardiovascular disease is present is not a simple matter which can be answered by a direct, unequivocal yes or no. Aging in itself seems to be accompanied by slight diminutions in efficiency which are accepted today as a part of the normal process of growing old. In many instances, cardiac illness seems to differ only in degree from normality. Perhaps the correct question to put to the clinician is not, "Does this patient have cardiac disease?" but rather, "What percentage of cardiac efficiency is retained by the patient? Is this patient's heart as efficient as the hearts of most persons of his age group?"

If possible, each patient should have a careful, routine and thorough examination early in life during a period of good health. Such an examination should include an x-ray film and an electrocardiogram. Serial studies on the individual patient are far more valuable for diagnostic and prognostic purposes than the comparison of a single examination with standard tables. If an early study is not available for an individual patient whose cardiac condition borders on the normal, the best plan is to re-examine the patient after an interval to determine the trend.

PRESIDENT LEE — Dr. Griffith, thank you very much for that magnificent presentation.

Now, are there any questions that anyone would like to ask of Dr. Griffith? If so, we should appreciate your giving your names when you rise to ask a question.

DR. GAMBER F. TEGTMEYER — As you probably know, Dr. Griffith, chest pain is one of the most important things we, as medical directors, have to assess in our work in selecting life insurance risks. You have given us a fine exposition of the subject, and you have brought out the importance of the "short leg syndrome" which I think is not very familiar to many of our men. Would you be good enough to elaborate on the "short leg syndrome" as it refers to chest pain?

DR. GRIFFITH — The son of A. B. Carnett, Professor of Surgery at the University of Pennsylvania Graduate School, suffered attacks of pain in his lower right quadrant. His appendix was removed, but the boy still had attacks of pain in the lower right quadrant. When examined, the boy was found to have parietal tenderness over the distribution of the right first lumbar nerve. Further examination disclosed that his right leg was an inch shorter than his left leg, resulting in tension of the dorsospinal mass of muscles, and chronic injury to the radiculi of the first lumbar nerve and a corresponding state of pain and tenderness over the distribution of the third, fourth and fifth intercostal nerves. After an elevation was placed on the heel of the left shoe, the pain disappeared.

DR. WILLIAM H. SCOINS — Dr. Griffith, in the series of chest films that you took, what is the incidence of aortic plaques, and what is their clinical significance?

DR. GRIFFITH — In the group of patients between 40 and 60 years of age, presence of an aortic calcified plaque is indicative of aortic atherosclerosis. Such plaques were found in about 11 per cent of the films.

DR. RALPH R. SIMMONS — In the "short leg syndrome" accompanied by pain, can you demonstrate dermatome changes?

DR. GRIFFITH — Yes, absolutely.

PRESIDENT LEE — Thank you very much, Dr. Griffith. We hope you will be able to join us in our scientific as well as our social program.

Our next speaker is another friend of all of you, and an old acquaintance. Dr. John W. Gofman gave an outline of his work to our meeting at Colorado Springs year before last. He assured me that between the time of Carl Anderson's meeting and this many things would transpire, and they have.

At this time it gives me great pleasure to introduce to you Dr. Gofman, Professor of Medical Physics at the University of California, Berkeley, whose subject will be, "The Present Status of the Problem of Lipid Metabolic Disturbances and Their Relationship to the Genesis of Arterial Disease."

THE PRESENT STATUS OF THE PROBLEM OF LIPID METABOLIC DISTURBANCES AND THEIR RELATIONSHIP TO THE GENESIS OF ARTERIAL DISEASE

JOHN W. GOFMAN, M. D.

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As our study of the relationship of serum lipoproteins to vascular disease has progressed, it has become increasingly apparent that the problem represents two major subjects. The first is that concerned with the metabolic derangements which result in deviations of the serum lipoprotein levels from the "normal". The second is that of the development of atherosclerotic vascular disease which in all likelihood arises incident to the disturbance in serum lipid transport. While it cannot be proved conclusively from present evidence that the latter statement is correct, the concept implied therein provides what to us appears to be the most fruitful working hypothesis at the present time.

Metabolic Aspects of Serum Lipid Transport

The blood occupies a central position in the metabolism of lipids, inasmuch as it represents a vehicle for the transport of lipid materials from sites of production and storage to sites of utilization and excretion. There may occur, in addition, certain very important transformations of lipid entities within the blood compartment. Thus, ultimate understanding of abnormal lipid metabolism must embrace this transport phase. As it has turned out, the blood transport phase may provide us with invaluable clues to the lipid metabolic defects themselves. The lipids of the blood exist in the form of structures very large on a scale of molecular dimensions, the smallest that contains any appreciable proportion of the total lipid content being of the order of the size of a serum albumin molecule. Secondly, these structures containing the blood lipids usually have several types of lipid materials (e.g., cholesterol, fat, etc.) present in a single structure, and these lipid materials are in some way bound to protein. Hence the term lipoprotein has come to characterize the entities transporting the largest propor-

tion of the lipid materials of blood. In our experience the ultracentrifuge has proved to be a tool of great power in characterizing serum lipoprotein composition and probably gives us a picture of the entities present which is very close to that which actually exists in the living organism. The earlier studies of Cohn, Oncley, and their coworkers had shown, by chemical fractionation procedures, that two major classes of lipoproteins existed, characterized as alpha and beta lipoproteins. Through the ultracentrifugal investigations of our group it has become apparent that each of these classes is complex. The "alpha lipoprotein" consists of at least three distinct species; the "beta lipoprotein" consists of a very much larger number of species, perhaps of the order of thousands. The lipoproteins may be segregated further on the basis of the physical property of density. Within the "alpha" group there exist lipoproteins of density 1.15 Gm. per cc., 1.075 Gm. per cc., and 1.05 Gm. per cc. Within the "beta" group there exists a spectrum of lipoproteins ranging in density from approximately 1.035 Gm. per cc. down to several of density less than 1.0 Gm. per cc. The density differences among the lipoproteins are ascribable in the main to differing contents of several lipids and of protein.

In ultracentrifugal analysis the density differences extant among the lipoproteins is very useful since they can be made the basis for separating and analyzing the various components present in a single serum sample. In the ultracentrifuge the driving force for sedimentation or flotation is proportional to the difference in density between the solution and the component under consideration. Thus, substances of density less than that of the solution in which they are suspended will undergo flotation toward the center of rotation, whereas those of density greater than the solution will undergo sedimentation away from the center of rotation. Therefore by the simple expedient of altering solution density by addition of low molecular weight electrolyte or non-electrolyte, one can cause flotation or sedimentation of a chosen segment of the entire lipoprotein spectrum. With the incorporation into the ultracentrifuge of a schlieren optical system, it is possible to quantitate not only which density classes are present in a sample but also to determine the concentration (in mg. per cent or any other desired units) of the various lipoprotein classes. While it

would be entirely appropriate to name the various lipoproteins present in blood by the density property, it is convenient to use another property, namely the rate of sedimentation or flotation under defined conditions in the centrifuge. The customary unit for describing such rates is the Svedberg, or S, unit for substances which sediment. For those which undergo flotation we have adapted this unit to the notation, the S_f unit (Svedberg of flotation). Thus instead of characterizing a lipoprotein as having a density of 1.03 Gm. per cc., we may refer to it by its flotation rate in a given medium (our conditions for low density lipoproteins usually being a medium of density 1.063 Gm. per cc. at a temperature of 26° C.) in terms of Svedbergs of flotation, e. g., S_f 6. Utilizing this general system of procedure it is possible to describe lipoprotein transport quantitatively in the human in health and in disease. In the course of this work it has been possible for us to improve our analytical methods in ultracentrifugal studies by quantitatively accounting for the self-slowing of lipoproteins with the result of sharpening the findings considerably.

The Systematics of Lipoprotein Transport in the Human

The study of large numbers of individuals of a large age range and of both sexes, both in health and disease, has revealed that there is a remarkable degree of order in the distribution of the serum lipids among the various possible lipoprotein classes. This order, or regularity, is of such degree that metabolic errors in the handling of lipids reflect themselves in deviations of the serum lipoprotein pattern from the normal for a given age and sex. Of great importance is the fact that such errors in metabolism can be determined even when there is no abnormality evident in the total level of a single component of the lipoproteins. Thus at a level of serum cholesterol of, for example, 250 mg. per cent, one individual's lipoprotein transport may be utterly different from that of another, reflecting a gross difference in some feature of metabolism involved in the handling of lipid substances. This may be true at any level of serum cholesterol or at any level of total serum lipid.

In the child in health the blood is characterized by having present at appreciable concentrations only the high density lipoproteins (the "alpha" group) and the lowest members of the low-density

series of lipoproteins, i.e., those of flotation rates of S_f 4 and S_f 6. The successively higher members of the lipoprotein spectrum (i.e., S_f 8, S_f 10, S_f 13, etc.) appear in increasing concentration in the serum of humans of both sexes with increasing age. "Aging" in this regard is an average trend, so that even when the average individual shows a progressive alteration with age, specific individuals at age 20 or 30 years may be characterized by having a serum lipoprotein spectrum like that of the average individual of 5 years of age. Up to the age of 20 years there is not any marked difference in the lipoprotein spectrum between the sexes, but thereafter the male sex "ages" lipoproteinwise much before the female sex, such that above age 20 the average male shows higher serum concentrations of the successively higher members of the lipoprotein spectrum (on an S_f scale) than does the average female. Roughly one may state that the thirty year old male has on the average reached a plateau in lipoprotein distribution, which plateau is not arrived at by the average female for another twenty years, i.e., at age 50 years. Even at the ages of 50 to 70 years certain individuals are still characterized by a lipoprotein distribution in the serum resembling that of the child or young adult. It is evident that the alteration in lipid metabolism which reflects itself in increasing concentrations of the steady-state level of the successively higher S_f classes of lipoproteins is by no means an *inevitable* concomitant of chronological aging. Further, several intercurrent disease states may develop which will alter markedly the orderly age progression. Among these are nephrosis, hepatitis, myxedema, diabetes mellitus, obesity, biliary obstruction, and probably a host of others. We would not consider that atherosclerosis is one of these, but rather is a disease that results from alteration in lipoprotein metabolism.

Thus far we have described simply the observable alteration in lipoprotein distribution as a function of age in the human. A more intimate view of the metabolic significance of this change in lipoprotein distribution requires some consideration of the composition of the various lipoproteins and of the transformations which they undergo. In this area our knowledge is largely the result of the investigations of my colleagues, Lindgren, Freeman, and Nichols. Lindgren has developed technics of isolating lipoproteins of narrow S_f bands by making use of separations based

upon density differences in the preparative ultracentrifuge. With such isolated lipoprotein preparations these workers have been able to analyze (chemically and by infra-red spectroscopy) the several lipid constituents and the protein of the various lipoproteins. Broadly their results may be summarized as follows.

As we pass from lipoproteins of low S_f classes to those of successively higher classes, these alterations occur:

a. The percentage composition of neutral fat within the lipoprotein increases progressively until at S_f 100–S_f 40,000 it has become the predominant constituent.

b. The percentage compositon of cholesterol drops progressively and, further, there is a shift from predominantly esterified cholesterol to free cholesterol.

c. The percentage composition of phospholipid drops progressively.

d. The percentage composition of protein drops progressively.

From these data we may translate the originally described age progression into one where individuals show higher and higher concentrations of the lipoproteins rich in neutral fat with aging. Since the lipoproteins can be demonstrated to have short average lifetimes in the blood, it may be concluded that an elevation in the steady-state level of any specific class is a reflection of an imbalance between the rate of influx of that class into the blood and its rate of efflux from the blood. A variety of experiments conducted by our research group has indicated both in the human and the experimental rabbit that normally lipoprotein transformation is in the direction of the higher S_f classes being converted to successively lower classes. In chemical terms this is consistent with the removal of a part of the neutral fat (glyceryl ester) of the high S_f classes, leaving a lipoprotein of lower S_f class (containing less glyceryl ester). A simple situation where this serial disappearance of high members with appearance of successively lower members occurs is in the blood of the human in the 24 hour period following the ingestion of a high-fat meal. If these data are incorporated into our considerations of the aging trend in lipoprotein patterns, the implication appears to be that, on the average, with age either for some reason a given load of lipoprotein in a high class is not being transformed at an adequate rate or that in

some way, from endogenous or exogenous sources, the effective load requiring transformation has been increased. In general the former possibility would appear the more likely, viz. that the rate of transformation through the serial classes has become slowed, with the result that the average level at the steady-state at a given age is increased over what it was in a younger age group.

If these considerations really reflect the mechanism of the altering lipoprotein distribution with age, it is evident that crucial information would reside in an understanding of the mechanism and agents responsible for the serial interconversion of lipoproteins. A partial block in the transforming system could explain the elevation of lipoprotein levels with age. The study of lipoprotein distributions chronically encountered in certain individuals indicates that such transformation blocks may occur at differing points along the sequence of lipoproteins such that differing segments of the lipoprotein spectrum may be included in the elevation observed in the serum level. Whether or not this means several *types* of block or differences in the severity of a single one is at present not clear. One lead in the possible elucidation of the nature of the transforming system has come through the investigations of the ability of parenteral heparin to effect clearance of the serum of the highest members of the lipoprotein spectrum with simultaneous increase in certain of the lower members. In vitro studies of this problem by Lindgren in our laboratory have shown conclusively that there is actual transformation of the high S_f lipoproteins, leaving over the lower classes. His work is not subject to the interpretation difficulty presented in the in vivo studies by the presence of the red blood cell phase and by the presence of vascular membranes across which potential transfer can occur. The work of Shore, Nichols, Lindgren, and Freeman in our group has demonstrated that there is a release of free fatty acid both in vivo and in vitro as a result of the action of the heparin-induced active principle on serum lipoproteins. Quantitative considerations indicate that the major and perhaps only source of this liberated fatty acid is the glyceryl ester moiety of the high S_f classes of lipoproteins. This would imply that heparin on injection has in some way resulted in the activation of a system, probably enzymatic, which is capable of hydrolyzing glyceryl ester. It is possible that the same system which is activated by heparin injection is that

which is normally involved in removing glyceryl ester from the high S_f classes of lipoproteins and their transformation into the lower classes. Present research is directed toward determination of whether or not defects in this particular transforming system are involved in the humans who fail to maintain normal lipoprotein patterns either in disease or with age.

Diseases Which May Be Related Secondarily to Elevation of Serum Lipoproteins

From present evidence it appears likely that such disorders as atherosclerosis and at least certain of the xanthomatoses result when adequately elevated serum lipoprotein levels have been maintained for a period of time. No real evidence has come to light which would indicate that atherosclerosis precedes or causes the lipoprotein elevation observed in individuals who have manifested a clinical sequel of it. The original concept of Virchow of an imbibition of lipids from the plasma into the vascular wall seems most promising, provided that it is tempered with the provisos that certain areas of the vascular wall are more susceptible than others and that certain lipids (as lipoproteins) are more likely offenders than others. That certain lipoprotein classes are elevated in individuals with manifest coronary artery disease over "normals" (i.e., individuals without manifest disease) has been amplified and confirmed since our earlier reports of this finding.

The two classes of lipoproteins we have previously demonstrated to provide independent association with atherosclerosis are the S_f 12–20 and S_f 20–100 lipoproteins. For future use in predictive work or in the clinician's hands for determining potential therapeutic effectiveness of an agent which alters or shifts lipoproteins, it is imperative that the relative strength of the relationship of each of these classes with atherosclerosis be determined and that any smaller contribution of other lipoproteins be taken into account. What is desired is a compendium of all the information that can be obtained from an ultracentrifugal analysis with respect to a single person's atherogenicity at the time he is studied. There exist methods capable of transforming the lipoprotein results into a single function which we may call an "index of atherogenicity", and which weights the concentration of each class of lipoproteins contributing to atherosclerosis according to the relative strength of its association with that disease. To this end

we have analyzed most of our ultracentrifuge runs by a new method we have been able to develop which takes into account quantitatively the slowing effect of lipoproteins upon themselves and other lipoproteins. The analysis accounts for all the low-density lipoproteins from $S_f 0$ to $S_f 400$, broken into several bands, and corrected for slowing effects. The four bands being studied currently are:

Standard S_f 0–12
Standard S_f 12–20
Standard S_f 20–100
Standard S_f 100–400.

The designation "standard" is applied to indicate that the bands considered are corrected for self slowing effects so that the positions of the S_f limits are corrected for this effect. This notation is necessary to distinguish these results from the older S_f 12–20 and S_f 20–100 which were not so rigorously corrected for this slowing effect. Utilizing this more rigorous approach to the analysis of ultracentrifuge runs, a comparison has been made of two series of individuals with coronary disease as compared with normals of the same age and sex. This study to date indicates that the relative strength of association with atherosclerosis is between 1.5 and 3.0 times as great for the band of Standard S_f 20–400 as it is for Standard S_f 0–20. It has not yet been possible to break down the data into the relative strength of the subsegments within these two bands. In determination of the atherogenic index one would use the following equation:

1 × Standard S_f 0–20 plus 2.25 × Standard S_f 20–400 equals the atherogenic index. Here the average factor of 2.25 has been used combining the determinations which gave 1.5 and 3.0 respectively. It is interesting to note that the factor of 1.5 resulted from the analysis of a 50–60 year age group whereas the 3.0 factor resulted from the analysis of a 40–50 year age group. It may very well turn out that this is not just a sampling error and that the two factors are inherently different. This would mean that the coronary vascular tree behaves differently with respect to these bands of lipoproteins as a function of age. In our current studies, similar determinations are in progress on the 30–40 year age group and the 60–70 year age group, in addition to adding many more cases to the two intermediary age groups. These studies should

help settle the question as to an age variation in the relative strength factors for the association of the lipoprotein bands with atherosclerotic coronary artery disease.

The determination of these relative strength factors, while important for maximal utilization of the data for predictive or prognostic purposes, has an importance beyond this for the clinician who wishes to use the information in prophylaxis or therapy. If, for example, a drug agent is developed which results in a shift of one class of lipoproteins into another, it would be pertinent to know whether or not the shift has been toward lipoproteins of intrinsically greater atherogenicity than existed before therapy. Combining the magnitude of the shift with the strength factors would enable one to determine whether or not the agent may be expected to be beneficial in atherosclerosis.

PRESIDENT LEE — Well, Gentlemen, I think you will agree that we have the authority on that subject, and we are very grateful to you, Dr. Gofman, for being with us and giving us this splendid up-to-date story on this subject. Now here again we should like to welcome any questions. Dr. Gofman says he will be glad to answer them.

DR. C. COLEMAN BERWICK — We have been watching with a great deal of interest Dr. Gofman's work, and I should like to ask a question of Dr. Gofman. We supplied a number of blood specimens to him and some were from patients with arteriosclerosis and coronary artery insufficiency. One man was so ill with coronary artery disease that he could not walk across the floor. His normal cholesterol was high, but Dr. Gofman reports a low ratio. I am wondering how that can be accounted for, Dr. Gofman.

DR. GOFMAN — We have always indicated that we have a certain number of cases that we cannot account for. If you ask why this man has a high cholesterol and low lipid protein level, well we do have men with coronary disease without having these substances in their blood. I would say that at least fifteen per cent of our cases of coronary disease studied do not fit the overall picture. All we have ever claimed is that we have a very significant statistical elevation.

In answering the question of why they do not fit, I think one of the things that we must look back on is that we know men will

have coronary occlusion and have a small plaque in a critical region. These people do not have much of a metabolic abnormality. They have some local factor in one coronary artery. As a result of this bad anatomical or other factor responsible for this portion of the coronary artery becoming involved, the artery is occluded, and they are not fortunate enough to develop collateral circulation in time, or they develop a myocardial infarction and become classified as coronary disease. We then jump one step further and say they are classified as coronary atherosclerotic. They may not be very atherosclerotic. They have only a local region that has got them into trouble and they do not fit the hypothesis. Well, the focal character of atherosclerosis has been recognized by the earliest investigators of the pathology. We must always keep this in mind, that if we try to study atherosclerosis we use clinical coronary disease as our criterion group. We are not using a group of which we can say, "All the patients in this group are highly atherosclerotic and all normals are not." There is an overlap.

We studied men who ten years ago had coronary occlusion, some of whom have accidentally lost 30 or 40 pounds of weight, or even 20 pounds of weight. Our earliest studies indicated that weight change did not have a big effect on the 10 to 20 class of lipid proteins. Subsequently, we were able to evaluate some higher classes of molecules — the 20 to 100 class of lipid proteins; and, in fact, over the last year or more we have been measuring the 10 to 100 band. We keep them separate — the 10 to 20 and 20 to 100 — because we think they represent different disorders and because we are not sure that the actual weighting factor is exactly the same.

We are trying to determine this by statistical methods. But in the 20 to 100 class of lipid proteins we have found that there is a very significant association with overweight. When I say a very significant one, I mean statistically significant. This means that there exist some individuals who are overweight and who will have maybe a twofold or threefold reduction in these lipid proteins if they lose 20 pounds of weight. But there exist other individuals who are thin and who have high levels, and still others who are obese and have low levels, and still another category of obese ones with high levels who will not respond to weight reduction.

Overall, we could say that, at least statistically, 10 to 20 per cent of the elevation in the 20 to 100 class of molecules is associated

with overweight, and it may well be that some of the people whom we have studied who have had coronary occlusion in the past may have been overweight before. At the time they developed their primary coronary disease — atherosclerosis — they had a higher level of lipid proteins. We see them now after the weight reductions and they do not have the higher levels, or I should say we see them at a considerably later age.

I think we should take into account these factors — the possibility that there was some change in the level from the time the man develops his disease to the time we see him, and the fact that there is also left over a small residue (although we ought to pick it up by, say, a Wassermann) — a small residue of coronary disease which is associated with syphilis. There is a small residue of coronary disease associated with rheumatic heart disease. It is not clinically diagnosed as rheumatic, and we are going to find coronary arteries not atherosclerotic at all.

I think we are satisfied that the percentage exception to the rules that we find does not in any way cause us to worry about the validity of our general concept in relation to these lipid proteins with atherosclerosis.

Dr. Karl Anderson — I should like you to comment on some new information that seems pretty important to me. Our friend, Dr. Ancel Keys, has just returned from a year's intensive research in Europe from which it appears that the total mortality rates of men of equal age is much less in most countries than in the United States, and that this difference is even greater when mortality rates from all heart diseases are compared. For example, the rate in the United States is about three times as high as in Italy for men of equal ages from 35 to 65 years.

Now, Dr. Keys also found two other things. The average Italian gets only about 20 per cent of his calories from fats as compared with the American who gets 35 to 40 per cent of his calories from fats. Finally, in a study of a sample of clinically healthy men, it was found that serum cholesterol in young men is about the same there as here, but that after age 30 or 35 years the serum cholesterol fails to increase with age in the Italians as it does here in the United States.

Something like the same thing was found in poor men in Spain, with the additional fact that men of the rich professional class, who eat a lot of fat, were no different from men in Minnesota in regard to cholesterol in the serum. Dr. Keys says that he thinks two factors are involved both in the serum level and in the incidence of heart disease. First, he puts the total fat intake in the diet. And, second, he thinks the total calories, and resulting obesity, have an influence. What do you think?

DR. GOFMAN — These studies we made on xanthoma tuberosum, and these lesions which you can see for yourself, lead me to believe that that phase of the disease is distinctly reversible. If someone asks me the direct question, "Therefore, can you say that the same thing is true about those lesions that are similar in the coronary arteries," my answer is, "No, I cannot say it." But I am so encouraged by these observations in the skin that I think it would be folly to give up the fight on coronary disease. I think there is every reason to believe that we can reverse it. But, on the other hand, from these finger casts of a woman who has had xanthoma tuberosum for several years you see one of the people who has defied statistics and managed to survive for ten years. These lesions of the earliest vintage in the skin of her elbows have become fibrotic. There is not much lipid in contrast to her fingers, and these lesions responded minimally to the treatment. The fibrotic lesion does not respond very much, but the lipid filled lesion goes down in volume and may disappear entirely with treatment.

So this could go on in the coronary arteries and we can reverse it, but we have no proof today that we have reversed it.

In respect to the question of the fat content of the diet, I think Dr. Keys' observations on the serum cholesterol and the relationship to diet are certainly correct. I think Snapper has pointed this out to us in some studies he made in China. He said the people in China who have coronary disease are those who can afford a better diet than the ordinary Chinese. We studied 200 Japanese people from the ages of 40 to 60 years. There are many factors, but the Japanese say that coronary disease is nowhere near the problem there that it is here. We studied 200 Japanese, and their average cholesterol was roughly 60 per cent of the average cholesterol serum in men of this country, and their average level of lipid

proteins was about half the level of normals in this country. Therefore, I should expect they would have less vascular disease. However, even though the fat content of their diet is lowered, I think there is one other factor; the average Japanese is 20 pounds lighter for a given height than the average American of a reasonable economic status. They just do not get as many calories to eat.

We know the fat content of a diet can affect the blood lipid level, and the relationship is not very high. Also, the state of obesity will increase the level of certain of these classes. It may be that both of these operate in the Japanese, and possibly also operate in some of the European groups that Dr. Keys has mentioned.

Dr. Anderson — I want to ask your frank opinion about the value, for individual diagnosis or prognosis, of measurements of lipoproteins or cholesterol, or both. Dr. Ancel Keys has, as you know, published several papers on the problem of discriminating between healthy people and those who show evidence of having severe degrees of atherosclerosis. A number of mathematical experts have agreed that his analysis is sound.

Now this analysis indicates that if we examined a thousand men, including one hundred men with clinical coronary heart disease, the use of the ultracentrifugal flotation method to discover the coronary patients would make far more errors than correct discriminations. If a critical level is chosen which will be exceeded by many of the coronary patients, a lot of healthy men would be excluded. In finding 50 patients, another 50 would be missed and a false positive diagnosis would be put on 150 or more healthy persons.

Dr. Keys says that the situation is just about the same whether we use lipoproteins, S_f 12–20 particles, phospholipids, total cholesterol, or uric acid measurements. All of these seem to show much the same discrimination between the averages of groups of patients and healthy men, but they all seem equally useless for individual application except for the rare extremes when the serum level is very high.

Is there, then, any sense in making any of these measurements in order to advise individual patients? And, if we are going to make any measurement for this purpose, is there any real statistical evidence that one method is better than another?

DR. GOFMAN — We have accumulated a lot of blood patterns, and with abnormal patterns we have been very interested to get in some follow-up studies. A lot of people who have passed a thorough physical examination with normal electrocardiogram, normal chest film, are found to have abnormal blood patterns. Frankly, I would not insure them, but they are normal. Some of these people actually have blood that is characteristic of xanthoma tuberosum and they definitely have normal electrocardiograms and were examined by competent people.

The complete story on that, on how well we can predict, we shall have in the course of the next year. A large survey is being conducted with the public health service, and I would not claim, or I would not like to claim, anything for it now except that the preliminary findings with the smaller number of followed cases are definitely in line with our observations on coronary disease.

There is no question but that persons can have a very abnormal blood pattern. With respect to the cholesterol determination, I think that this is definitely of value. I think the lipoproteins show us many things that cholesterol determination would not show. We can take two people with 600 mg. of serum cholesterol and they have different diseases, as different as night and day. Nevertheless there is a correlation between the cholesterol and the lipoproteins, and the cholesterol determination is valuable if done in good hands. We have fought with this problem of cholesterol determination for a few years and we know if we get a cholesterol of 250 mg. that the cholesterol is between 240 and 260 mg.

I think a cholesterol determination once a year would be very valuable. At 20 to 25 years of age most men have good blood values, but at 30 and 35 years of age a lot of men have broken over into abnormality.

PRESIDENT LEE — Dr. Gofman, I want to thank you for being with us and for this very wonderful presentation. You are an old friend of this organization, and we hope you will be back again.

It is with very great pleasure that I introduce to you now Dr. Myron Prinzmetal, Associate Clinical Professor of Medicine, University of California School of Medicine, Los Angeles, who will speak to us about "Irregularities of the Heart Beat." Dr. Prinzmetal.

THE NATURE AND TREATMENT OF THE AURICULAR ARRHYTHMIAS*

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A series of studies has been conducted in this laboratory on the auricular arrhythmias in the experimental animal and in the human. These observations have suggested that the widely accepted theory that the auricular arrhythmias result from a circus movement is erroneous. The classic studies of Lewis and his associates were based entirely upon electrocardiographic observations, while in the present investigation two recently developed instruments, the high-speed cinematograph and the cathode-ray oscillograph, have been employed. Definitive evidence of the course of events occurring in the auricles was obtained by 1) tracing the auricular excitation wave by means of direct or semi-direct leads from multiple sites on or adjacent to the auricular surface, and 2) recording the auricular contraction wave in high-speed cinematograms. These two direct methods of observation have been extensively employed in experimental animals. In humans, the operations of atrial appendectomy and mitral commissurotomy have enabled us to study the exposed auricles of several patients during episodes of spontaneous auricular flutter or fibrillation.

The present discussion will include 1) observations made on the experimentally produced auricular arrhythmias in the dog, 2) a description of the findings in patients with spontaneous flutter or fibrillation, 3) a brief comparison between observations in man and experimental animals, and 4) pharmacologic considerations.

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*The work described in this report was performed in collaboration with Jacob Bernstein, M.D., Isidor C. Brill, M.D., Eliot Corday, M.D., Joshua Fields, M.D., Walter Flieg, M.D., Harold Karpman, A.B., Rexford Kennamer, M.D., H. E. Kruger, Robert W. Oblath, M.D., John A. Osborne, M.D., Alvin L. Sellers, M.D. and L. Allen Smith, M.D. Studies on the human auricles during surgery was made possible through the courtesy of Dr. Alfred Goldman.

From the Institute for Medical Research, Cedars of Lebanon Hospital and Department of Medicine, UCLA Medical School.
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EXPERIMENTAL OBSERVATIONS

Experimentally, any or all of the arrhythmias were initiated by either electrical, chemical, or mechanical stimulation which set up an ectopic focus discharging at a given rate. Regardless of the method of production, the rate of discharge of the ectopic focus determined which arrhythmia occurred. Relatively slow rates of discharge caused premature auricular systoles and paroxysmal auricular tachycardia, while the faster rates resulted in auricular flutter or auricular fibrillation.

Auricular Fibrillation:

Motion Picture Observations: Auricular fibrillation produced in the experimental animal is characterized by two phenomena in motion pictures: 1) Minute irregular contractions that are continuously present, and 2) large rhythmic, wavelike contractions.

The minute contractions cannot be seen with the unaided eye but reveal themselves on the high-speed films. They occur constantly throughout the auricular musculature and involve an area of auricular wall approximately 0.03 to 3.0 mm. in diameter. Superimposed on this sea of small contractions are large, moderately vigorous contractions that sweep across the auricle in a fairly regular wavelike manner at rates of about 400 to 600 per minute. The "fibrillation" of the auricle that is visible to the unaided eye is due to these larger contractions. These contractions are fairly uniform in time but not in strength. In cinematograms taken at 2,000 frames per second, the activity is so slowed that if these large waves pursued any type of main circular pathway, such would be readily visible. However, careful investigation of these slow-motion pictures taken of both auricles, individually and together, failed to reveal a main circular pathway. In extremely magnified pictures of a part of the auricle, as small as one square centimeter in area, no minute circus movements were seen. The individual muscle fibers contracted in a chaotic and irregular manner.

A variety of specific experiments designed to block the hypothetical circus path (burning, cutting, and the like) has been performed. These experiments have confirmed the visual evidence for the absence of circus movement.

Electrocardiographic Observations: The electrical activity in auricular fibrillation was investigated by electrocardiography and oscillography. In direct auricular leads, small, rapid, irregular deflections are found on the larger undulations. These small waves of electrical activity may be related to the minute contractions seen on the motion pictures; on oscillographic tracings they number as high as 20,000 per minute. The minute waves are seen only in auricular fibrillation, and indirect evidence has been obtained which indicates that these small, irregular waves are largely responsible for the irregular ventricular responses characteristic of this arrhythmia. In ordinary electrocardiograms of auricular fibrillation, the minute waves may cause tiny, rough irregularities in the "f" waves. In the ordinary electrocardiogram the familiar "f" waves probably represent the large contractions.

Simultaneous records from two closely adjacent unipolar electrodes placed at numerous selected points on the surface of a fibrillating auricle show that all waves are arrhythmic and are usually unrelated in frequency or amplitude.

When electrical stimulation is used to produce auricular fibrillation, auricular rates of 400 to 600 usually must be achieved. The rate at which fibrillation occurs can be designated as the fibrillation threshold. Studies on auricular conduction recovery under a wide variety of circumstances, indicate that the fibrillation threshold is influenced by the state of auricular conductivity.

Auricular Flutter:

Motion Picture Observations: Motion pictures of the auricles, during auricular flutter reveal regularly recurring contraction waves arising at an ectopic focus. With electrical stimulation, auricular flutter occurs at auricular rates of 300 to 400 per minute. The flutter waves are similar to the large waves seen in auricular fibrillation but are more regular and generally more vigorous. No minute contractions are seen in auricular flutter.

Slow motion pictures were taken of both auricles simultaneously during auricular flutter. The films were projected so that motion was slowed 250 times. If a circus movement were present, one appendix should be seen to contract many seconds before the other on films taken at this speed. However, it was clearly seen that both appendices contracted at nearly the same instant.

When auricular flutter was produced by applying aconitine locally at the center of the wall of the right auricle, the contraction waves were seen to originate at the ectopic focus in a perfectly rhythmic manner, and to spread over the auricles in all directions at once. No circus movement of the wave of contraction could be seen and no daughter waves were present. Interruption of the hypothetical circus pathway by burning or cutting did not in any way interfere with the auricular flutter contraction wave.

It thus appears clear that the mechanism of auricular flutter is not a circus movement; for, if it were, the contraction wave would have to pursue a unidirectional path around the cavae. The films show that this is not the case; each contraction wave takes its origin at the ectopic focus, and, instead of traversing the auricle in a single direction, actually spreads from the focus simultaneously in all directions.

Electrographic Observations: Lewis' evidence for circus movement in flutter is based on timing the intrinsic deflections with direct auricular electrodes. However, a considerable gap in Lewis' hypothetical circus path exists since, by the technic in general use at that time, the body of the left auricle could not be exposed sufficiently to allow adequate investigation in that region. Therefore, it seemed advisable to analyze the intrinsic deflections in both auricles, including the heretofore unexplored gap (the body of the left auricle), and thus test our cinematographic conclusions by Lewis' own method.

By means of extensive dissection, both auricles were explored, including the body of the left auricle, in 30 dogs. Completely consistent results were obtained as described in the following experiments.

Experiment 1. — Aconitine was placed in the natural crevice between the inferior vena cava and the pulmonary vein from the left lower lobe. Electrodes were placed equidistant (2 cm.) from the aconitine focus, one electrode on the body of each auricle respectively.

If a circus movement were present, the impulse would arrive at the electrode of one auricle an appreciable time (at least 0.15 second) before it reached the other. It was found that this was

not the case; the impulse arrived at both electrodes nearly simultaneously (within 0.005 second).

Experiment 2. — Aconitine was placed at the same point as in Experiment 1. Paired fixed electrodes were placed on the body of the right auricle, one at a point 1 cm. from the aconitine focus, the other at a point 4 cm. from the focus. It was found that the impulse arrived at the more distal electrode at a significantly later time than at the proximal electrode.

The same procedure was now repeated on the left auricle in the same animal. The paired electrodes were transferred to analogous positions on the body of the left auricle. The timing of the respective intrinsic deflections clearly demonstrated that the course of the impulse in the left auricle was in the same direction as in the right, i.e., away from the aconitine focus.

This finding is of crucial importance since, if the impulse were pursuing Lewis' circus path, it should on its "return journey" travel toward the aconitine focus instead of away from it.

Thus, when the course of the impulse over the heretofore unexplored gap (body of the left auricle) is charted, the circus movement theory is shown to be invalid.

Experiment 3. — Aconitine was placed in the center of the body of the right auricle. After flutter was produced, an electrode was placed on either side of the focus and equidistant from it. It was found again that the impulse arrived at each electrode simultaneously.

Thus the cinematographic and electrographic studies just described establish that auricular flutter in the animal consists of rapidly recurring waves which spread outward from the ectopic focus in all available directions. The configuration of the auricular flutter wave of the electrocardiogram has been elucidated by these studies. It was found that if the ectopic focus is located at the caudal end of the auricles, an inverted P′ wave is inscribed in limb leads II and III. If the excitation wave originates in the cephalic region, an upright P′ wave in leads I and II is recorded.

These studies indicate that the flutter wave is not a specific wave unrelated to other electrocardiographic waves. Rather it is a wave of depolarization, followed by a wave of repolarization. This second wave has been designated the T_A wave. It has been

found to gradually replace the isoelectric interval between complexes as the auricular rate increased. One of the most important factors influencing the size of the T_A wave is the auricular rate. At relatively low rates the P′ wave is followed by an isoelectric period. At more rapid auricular rates the P′ wave extends beyond the isoelectric line to form the first limb of the T_A wave; the second limb of the T_A wave returns to the isoelectric line. When the auricular rate is increased still further, the T_A wave becomes larger and more bowed until eventually it may usurp the entire space formerly occupied by the isoelectric period. The second limb of the T_A wave then joins the first limb of the P′ wave and thus forms the continuous undulatory pattern of flutter of the pure sine wave type.

Auricular Paroxysmal Tachycardia:

Auricular paroxysmal tachycardia was studied in the same manner as described above. Cinematographically, the contraction waves of auricular tachycardia appear similar to those of auricular flutter, but differ in at least three respects: 1) The auricular rate (the rate of discharge from the ectopic focus) in tachycardia is slower than in flutter; 2) As a result of this slower rate each auricular wave is followed by a ventricular response, that is, no AV block exists. The important difference in the two arrhythmias lies in the conduction system. In tachycardia there appears to be a firm bond between the auricle and the conduction system. Carotid sinus pressure and increased vagal tone cannot break this bond and cause AV block. In flutter (because of the faster auricular rate and other reasons which are unknown) this bond is already broken and AV block in varying degrees is (with few exceptions) always present; increased vagal tone increases the block. However, if either tachycardia or flutter occurs in the presence of complete heart block, this striking difference between the two arrhythmias is absent; 3) The propagation of the individual tachycardia wave is faster than that of the flutter wave. As in flutter, each tachycardia contraction wave originates in an ectopic focus in the auricular musculature and proceeds to invade the auricles in all directions simultaneously.

CLINICAL OBSERVATIONS

Clinically, auricular flutter and auricular fibrillation are closely

associated and commonly accompany the same disease states. Moreover, conversion from flutter to fibrillation or from fibrillation to flutter often occurs either spontaneously or in response to drugs. Nevertheless, electrical and mechanical activity in the auricles of patients during spontaneous flutter has been found to differ radically from the activity characterizing spontaneous fibrillation.

Auricular Flutter:

The mechanism of spontaneous auricular flutter in patients was studied by the methods of simultaneous multiple esophageal lead electrocardiography, precordial and limb lead electrocardiography, and high-speed cinematography.

Electrocardiographic Findings: At a distance of approximately 20 to 40 cm. from the lips, the human esophagus is in close association with both auricles. The esophageal region 30 to 37 cm. below the lips is at the midauricular level and is directly posterior to the interauricular septum. At the level of the extreme caudal end of the auricles, 37 to 40 cm. below the lips, the esophagus appears to be in more intimate contact with the right than with the left auricle. At levels 20 to 30 cm. from the lips, the esophagus is immediately posterior to the cephalic extremity of the left auricle. Although all portions of both auricles are not in direct contact with the esophagus, the distance separating these structures is so slight that electrical potentials in *both* auricles are recorded in esophageal leads from all auricular levels. Therefore, the course of the auricular impulse can be determined by analyzing the configuration of the depolarization waves in simultaneous esophageal leads. This has been accomplished in previous studies by other workers, as well as in the present investigation of spontaneous auricular flutter in man.

Most patients with auricular flutter exhibit inverted depolarization waves in limb leads I, II, and AVF. In these instances, representing the "common type" of flutter, esophageal leads from the caudal level of the auricles display a purely negative depolarization wave, esophageal leads from the cephalic level of the auricles present a purely positive wave, and esophageal leads from the midauricular level contain a negative wave followed by a positive wave. In the uncommon type of auricular flutter, in which the

depolarization wave is upright in limb leads I, II, and AVF, negative depolarization waves are recorded in esophageal leads from the cephalic level, and positive waves appear in esophageal leads from the caudal level; esophageal leads from the midauricular level exhibit biphasic deflections similar to those observed in the common type of flutter. Interpretation of these tracings is based upon the fundamental electrocardiographic principle that a negative deflection is inscribed as the cardiac impulse travels away from the recording electrode, while a positive deflection occurs when the impulse is traveling toward the electrode; a pure negative wave (called the intrinsicoid deflection) is recorded by an electrode at or near the site of origin of the impulse.

By applying the preceding principle, the esophageal lead electrocardiogram of spontaneous auricular flutter may be interpreted as follows: In the common type of flutter, the purely negative deflection recorded from the caudal level indicates that the impulse arises at and travels away from the caudal region of the auricles. Conversely, the positive deflection obtained in esophageal leads from the cephalic level establishes that the auricular impulse travels toward and terminates in the cephalic region. The biphasic deflection from the midauricular level shows that the impulse travels toward the middle of the auricle, passes beneath the recording electrode, then recedes from the electrode as it continues its journey to the cephalic extremity. Since electrodes in the esophagus record potentials in both auricles, the auricular impulse in these instances must originate from a caudal focus and travel in a caudocephalic direction through both auricles simultaneously. In the uncommon type of flutter, the impulse must arise in the cephalic region and travel through both auricles simultaneously in a cephalocaudal direction.

If a self-perpetuating circus movement were present in auricular flutter, as hypothesized by Lewis, identical deflections would be expected to occur in esophageal leads from all auricular levels, since the circular path would be without beginning or end. Hence the above findings are inconsistent with Lewis' concept of circus movement. If a circus movement arose anew with each cardiac cycle, as suggested by certain workers, the deflections in esophageal leads from various auricular levels again would differ radically from those described above. In the common type of

flutter, an impulse pursuing a circus pathway through both auricles would travel from the caudal region of one auricle to the cephalic extremity, where it would enter the opposite auricle and travel in a cephalocaudal direction on its return journey to the focus. Under such circumstances, electrodes in the esophagus at the caudal level of the auricles would register a negative deflection as the impulse traveled toward the cephalic region, followed by a positive deflection as the impulse returned to the caudal region. Similarly, esophageal leads from the cephalic level of the auricles would exhibit a biphasic deflection, consisting of a positive component recorded while the impulse traveled up one auricle and a negative component recorded during the return journey. Finally, an electrode at the midauricular level would register a positive deflection as the impulse traveled from the focus to the middle of one auricle, a negative deflection as the impulse passed the electrode and continued to the cephalic extremity, and a second positive-negative phase as the impulse traversed the opposite auricle. Equally complex deflections would be recorded in the uncommon type of flutter if a circus movement were present. Thus, assuming that the fundamental principles of electrocardiography are valid, the configuration of the depolarization waves in esophageal leads from patients with spontaneous flutter is entirely incompatible with the occurrence of a circus movement traversing both auricles. Moreover, the above findings are equally inconsistent with the existence of a circus pathway around the septum, within only one auricle, or involving any anterolateral portion of one or both auricles. A comparison of the times of onset of the intrinsicoid deflections in esophageal and precordial leads, as well as a calculation of the momentary atrial electrical axes in limb leads, likewise indicates that the excitation wave of spontaneous auricular flutter in man arises from an ectopic focus and pursues a linear rather than a circus pathway.

Cinematographic Findings: High-speed cinematograms of the exposed auricles have been recorded during mitral commissurotomy in a patient with spontaneous auricular flutter. Routine tracings from this patient exhibited inverted depolarization waves in limb leads II and III indicating that the arrhythmia was of the common type arising in the caudal region. The auricular flutter rate was 240 beats per minute. Films were recorded at a camera speed

of 100 frames per second and projected at a rate of 8 frames per second; hence the auricular contractions depicted on the screen were 13 times slower than the actual heart rate and occupied an interval of approximately 3.6 seconds per beat.

By pushing down on the pulmonary artery, it was possible to obtain films in which the motion of both auricular appendices was very clearly seen. If a circus movement had been present, either the left or the right appendix would have contracted before its fellow, depending on whether the movement were clockwise or counterclockwise. Indeed, assuming the distance between the two appendices constitutes one fourth of the hypothetical circus pathway, one appendix would have contracted about one second before the other. Actually, however, repeated examination of the cinematograms revealed that the two appendices contracted simultaneously. This phenomenon is entirely incompatible with the circus movement theory, but is consistent with the electrocardiographic observations described above. Cinematographically as well as electrocardiographically, therefore, it has been demonstrated that the excitation wave of spontaneous auricular flutter in man starts at an ectopic focus and spreads in a linear pathway through both auricles simultaneously.

Auricular Fibrillation:

Spontaneous auricular fibrillation in patients was studied by means of direct auricular lead electrocardiograms, esophageal and limb lead oscillograms, and high-speed cinematograms.

Electrocardiographic Findings: During operations on the mitral valve, direct auricular leads from 4 patients with spontaneous auricular fibrillation were recorded on the Sanborn Twin Beam Cardiograph. This photographic-writing instrument was operated at a paper speed of 75 mm. per second, yielding a much more accurate representation of the rapid electrical activity in the fibrillating auricle than is obtainable with standard electrocardiographic equipment. Examination of the tracings revealed slightly irregular waves varying from 0.2 to 0.4 millivolts in amplitude and occurring at a frequency of 350 to 400 per minute. Some of the waves presented a sharp downstroke resembling an intrinsic deflection. No two waves were identical in shape or size. These deflections presumably correspond to the familiar

"f" waves seen in limb leads of auricular fibrillation. In addition to the large waves, smaller waves of highly variable contour occurred at extremely rapid and irregular rates throughout the direct lead tracing, appearing as peaks or undulations along the baseline and on the upstroke and downstroke of the larger deflections.

Esophageal leads from 4 undigitalized and 20 digitalized patients with auricular fibrillation were recorded with the cathode ray oscillograph. Because of freedom from inertia, rapid recording speeds and virtually unlimited frequency response, the oscillograph proved even more satisfactory for purposes of the study than the photographic-writing cardiograph. In undigitalized subjects, esophageal leads from auricular levels revealed essentially the same phenomena as the direct leads described above. Large "f" waves, approximately 0.2 to 1.0 millivolts in amplitude, were recorded at frequencies of about 350 to 600 per minute. Small waves, usually 0.1 millivolt or less in amplitude, occurred at extremely irregular rates as high as several thousand per minute.

Simultaneous oscillograms from 2 electrodes placed 2.5 to 5 cm. apart in the esophagus revealed little or no synchronicity between the electrical activity in different parts of the fibrillating auricle. Esophageal leads from the digitalized patients exhibited deflections of much lower amplitude than records from undigitalized subjects but were otherwise essentially similar.

Cinematographic Findings: High-speed cinematograms of the fibrillating auricles were recorded in 4 patients during mitral commissurotomy and in 1 patient during auricular appendectomy. Because of the presence of mitral stenosis, the left auricles of these patients were distended and often filled with clot; this factor, coupled with digitalization, limited the motion of the left auricle. However, in the patients undergoing commissurotomy, excellent cinematograms of the fibrillating right auricular appendix were obtained by pushing down the pulmonary artery.

When viewed in slow-motion pictures, the right auricular appendix was seen to contract at an irregular rate of 350 to 400 beats per second. Each contraction appeared as a more or less organized wave differing somewhat from the preceding wave in course, vigor, and rate of propagation. Careful examination of the films further revealed a second type of mechanical activity oc-

curring simultaneously with the large contraction waves and consisting of rapid, heterorhythmic contractions and dilations of minute muscle segments throughout the appendix. These microscopic contractions were most readily discerned in the tip of the appendix where the fimbria twisted and turned first in one direction, then in another, in an entirely uncoordinated manner. Presumably the large contraction waves seen in the films correspond to the electrocardiographic "f" waves, while the miscroscopic contractions are mechanical counterparts of the small deflections recorded in direct leads.

From the preceding electrocardiographic, oscilloscopic, and cinematographic observations, it may be concluded that spontaneous auricular fibrillation in the patient is a heterorhythmic disturbance composed of irregular, large waves which pursue a variable course over a sea of asynchronously contracting minute muscle segments. Neither the tracings nor the films reveal any evidence of a circus movement, or of an "isoelectric gap" or "daughter waves" such as those hypothesized by proponents of the circus movement theory.

Relationship Between Clinical and Experimental Arrhythmias

Except for differences attributable to pathology and medication, the preceding observations on spontaneous auricular flutter and fibrillation in man are remarkably similar to findings obtained during a 4 year study of experimentally produced auricular arrythmias in dogs. Direct leads and high-speed cinematograms from numerous experimental animals have shown that auricular flutter consists of rhythmic waves traveling from a focus at one end of the auricles to the opposite extremity through both auricles simultaneously, and that auricular fibrillation consists of heterorhythmic activity comparable to the large and small waves recorded from the fibrillating auricles of patients. The existence of a circus movement in the experimental instances studied has been conclusively ruled out. Although the operation of mitral commissurotomy has greatly facilitated investigation of the human auricle, much remains to be learned concerning the relationship between clinical and experimentally produced auricular arrhythmias. Nevertheless, it is noteworthy that findings in a large series of experimental animals are essentially similar to the results obtained

by direct observation of spontaneous auricular flutter and fibrillation in man.

PHARMACOLOGIC CONSIDERATIONS

The present concept of the action of antiarrhythmic drugs, such as quinidine and digitalis, is that they act largely through their supposed effect on the gap between the head and tail of the circus movement. In the light of the above observations such a concept is untenable.

The principal pharmacologic action of quinidine is that it depresses both auricular excitability and auricular conductivity without influencing the absolute refractory period. This action at the ectopic focus decreases the rate of impulse formation and discharge. It is in this way that quinidine is effective in terminating all the auricular arrhythmias.

The effect of digitalis on the auricle consists of 1) a weak, direct action resembling that of quinidine, and 2) a more dominant, indirect action, exerted through an increase in vagal tone, which tends principally to affect auricular rate. This latter action tends to account for its effect in the various arrhythmias. When administered during an arrhythmia, digitalis exerts an effect similar to that of vagal stimulation or a cholinergic drug. Thus, an auricular tachycardia may be terminated, flutter is usually converted to fibrillation, and fibrillation is perpetuated. Although flutter and fibrillation are occasionally terminated, particularly if paroxysmal, the drug is usually administered in these latter two arrhythmias to accomplish ventricular slowing.

Much remains to be learned concerning the pharmacology of quinidine and digitalis; however, the effect of these drugs on the auricular arrhythmias can be explained without resorting to the circus movement theory.

PRESIDENT LEE — Gentlemen, anything I could say would not be worth while after that marvelous presentation. This is a big problem to us in the field of cardiology. Now, there must be many of you who would like to ask questions. I asked Dr. Prinzmetal if he would be willing to answer some questions as to practical applications here and I would like to see some discussion. I do not think you should be modest about asking some

simple questions which may have come to your mind during this demonstration.

DR. ARCHIBALD C. WILSON — My question has to do with fibrillation in young individuals. Most of the literature comments upon the benign type, where there is no significant history, no demonstrable cardiac disease, and the condition is believed to be benign. It seems to me that if it is a relatively common finding we can probably accept such a conclusion with a measure of statistical probability. Can Dr. Prinzmetal tell me if he has any ideas as to what proportion of this type of fibrillation would fall into the benign category.

DR. PRINZMETAL — I do not think any cause of auricular fibrillation is completely benign, but according to a large series of cases by Paul White and Isidor Brill about 4.6 per cent occur without known heart disease. Ninety-five per cent, approximately, occur with rheumatic and atherosclerotic heart disease, but one patient in twenty does not have heart disease.

If it is a very young person, you must be sure the patient does not have Wolff-Parkinson-White syndrome, because auricular fibrillation is one of the arrhythmias that occur in this condition. That certainly is not a benign disturbance, because patients die with arrhythmia. Paul White told me of a woman who died recently because of that. The difficulty with Wolff-Parkinson-White syndrome is that sometimes the QRS complexes appear to be perfectly normal. Sometimes it is very difficult to make this diagnosis, but if the P-R intervals are short between the paroxysms I think you can be fairly sure it is a form of the syndrome and I think it is a serious syndrome. We see many deaths in infants with this. It is sometimes very difficult to arrest and cure, and the best treatment is digitalis, not quinidine.

DR. JOHN J. HUTCHINSON — This may be a little off the subject, but I am interested in idiopathic bundle branch block. We have cases of it to underwrite. There is a difference of opinion as to just how to evaluate them, and I should appreciate any comment you might have on that.

DR. PRINZMETAL — Well, as so often happens in medicine, fifteen years ago they said bundle branch block had a life ex-

pectancy of two years. Now there are articles saying it has normal expectancy. I think the truth lies somewhere between the two.

Patients with left do not have such good life expectancy as patients with right bundle branch block. I think if you consider bundle branch block a structural disease it must be concluded that most cases have something wrong with the heart. But, if it is small enough and at the right spot, you can have a very abnormal electrocardiogram and a normal life expectancy. On the other hand, if it is very diffuse, the electrocardiogram can look the same and the prognosis can be poor. You have to decide about the prognosis by each individual case.

If the heart is large, the prognosis is worse; if it is small, it is better. If the bundle branch block occurred after an episode of precordial pain, the prognosis is worse than if it came idiopathically, because in the first case it probably was a result of some type of coronary disease.

Why is there a difference between the right and left bundle branch? Clinically, patients with right bundle branch block do better than those with left. I think the reason is that the coronary artery disease involves the left ventricle. So the etiology is different, perhaps, and the left bundle branch block involves the left part of the septum and, therefore, is a diffuse disease.

Dr. Berthold T. D. Schwarz — I would like to pursue the question that Dr. Wilson asked in respect to the benign fibrillation and the more malignant type. Apparently 4 to 5 per cent are functional and the others have an organic basis. Among those that had the organic basis, we know clinically the cases with fibrillation lived for a great many years. In that respect, what is the longevity to be expected?

Dr. Prinzmetal — I think it depends entirely on the underlying heart disease. If a patient with a severe coronary occlusion suddenly has fibrillation, death may occur within a half hour. On the other hand, a patient with mitral stenosis, well digitalized, well compensated, can have an auricular fibrillation for several decades. Again, it depends on the disease of the ventricles and not on the disease of the auricles.

The fibrillation undoubtedly makes the heart worse. If the patient can have normal sinus rhythm, he is better off than if he has fibrillation, especially with rheumatic heart disease. But the prognosis depends upon the myocardium and not on the arrhythmia.

DR. RALPH R. SIMMONS — Do you feel that digitalis is more efficient than quinidine because of the dilatation of the auricle with quinidine in fibrillation?

DR. PRINZMETAL — It depends on the circumstances. If it is a young person with paroxysmal fibrillation, digitalis is the drug of choice and may terminate the arrhythmia. If it is a person with a bad myocardium that suddenly starts to fibrillate, it is preferable to give digitalis before giving quinidine. One of the dangers of quinidine is that the ventricular rate is so rapid if they do not have digitalis first that it makes the heart failure much worse.

So, in older people with bad myocardiums it is best to use digitalis simultaneously with quinidine if it is urgent, and then use quinidine alone. In young people with good myocardiums, it does not make a great deal of difference.

PRESIDENT LEE — We have directed our discussion here toward auricular irregularities. Doctor, would you comment for a moment or so on ventricular irregularities? In a broad sense, what is your point of view about the significance of, for instance, ordinary ectopic beats under the influence of exercise, and so on?

DR. PRINZMETAL — I shall start by saying that ventricular tachycardia is always a very serious disturbance, and Strauss, as you may remember, found that persons with this condition lived a very short time. Even though the heart in ventricular tachycardia is not beating rapidly, it does not have normal contractions. The patient goes into shock, gets coronary insufficiency, and dies.

The next arrhythmia of the ventricles is fibrillation. The only ones of importance, clinically, are the paroxysmal fibrillations about which you must be careful. This is a rather unusual form of Stokes-Adams disease. If extrasystoles are multifocal, there is a worse prognosis than if they are unifocal. On the other hand, there are patients who have ventricular extrasystoles for 30 or 40

years and nothing seems to happen to them at all; and what the mechanism is of those I think no one knows. The group of patients with extrasystoles and small hearts and no other form of heart disease, if you can reassure them and tell them nothing is wrong, and do not give any medicine, get along fine. They sometimes get distressed when the blood pressure fails during systole. Outside of that circumstance, it is perhaps best not to try to do too much if the heart is otherwise normal.

UNIDENTIFIED SPEAKER — I am wondering how you would treat a case of ventricular tachycardia.

DR. PRINZMETAL — Again, it depends on a lot of things — whether the patient is in shock, how fast the ventricles are, and if the blood pressure is low. There are two drugs useful, quinidine and Pronestyl®. It was originally thought that Pronestyl® had great advantages over quinidine, but after more use they were found to have just about the same degree of toxic properties. I think the best drug is quinidine and I would give it intravenously, very slowly, while taking practically continual electrocardiograms. If the quinidine does not work, then use Pronestyl®. But the doctor has to watch the blood pressure because its use is associated with a very high mortality.

PRESIDENT LEE — If there are no other questions, Dr. Prinzmetal, I want to thank you on behalf of our group again for your kindness in coming here, and we hope your charming wife and you will join us this evening.

Our next speaker is from Canada. I should like to express my appreciation and that of my associates for the splendid representation of you fine folks from Canada. I need not tell you of the history of the Canadian group and of their contributions made in the past and which they are now making. Dr. Francis A. L. Mathewson, Medical Director of the Great-West Life Assurance Company of Winnipeg, is Assistant Professor of Medicine at the University of Manitoba and Consultant Cardiologist to the Royal Canadian Air Force. His subject is "Prolonged P-R Interval in Apparently Healthy People." We are indeed happy to have you with us, Dr. Mathewson.

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PROLONGED P–R INTERVAL IN APPARENTLY HEALTHY PEOPLE

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It is the purpose of this paper to describe the characteristics of A–V conduction observed over a period of years in the electrocardiograms of 57 apparently healthy persons exhibiting a P–R interval exceeding 0.20 second.

The mechanism of auriculoventricular conduction has been investigated in both the experimental animal and man and the changes it may undergo have been documented by such workers as Lewis (1, 2), Meakins (3) and Wilson (4). Extensive references to this subject up to 1925 are to be found in Lewis' "Mechanism and Graphic Registration of the Heart Beat" (5). These studies, which for the most part were concerned with acute experiments and observations over short periods of time, form the basis of our present understanding of A–V conduction and the variations it may undergo in response to both physiologic and pathologic influences.

There are both direct and indirect references (6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16) to the fact that a prolonged P–R interval may occur in the electrocardiogram of individuals who show no apparent disease. Some idea of the frequency of this finding may be gathered from the reports (17, 18, 19, 20, 21, 22, 23, 24) of electrocardiographic surveys of large groups of apparently healthy people, particularly in connection with military and civilian flying. The frequency recorded in selected reports is shown in Table I.

TABLE I

FREQUENCY OF P-R INTERVAL GREATER THAN 0.20 SECOND IN THE ELECTROCARDIOGRAMS OF APPARENTLY HEALTHY PEOPLE

Author	Number in Study	P-R Interval >0.20 Second	
		Number	Percent
Carlen. Unpublished RCAF report 1944	1,000	13	1.3
Ferguson & O'Connell 1926	1,812	26	1.5
Graybiel, et al 1944	983	16	1.6
Hall, et al 1942	2,000	31	1.6
Mathewson & Sellers 1946	324	10	3.1
Mathewson, et al to be published	971	15	1.5
McFarland, et al 1939	173	3	1.7
Stewart & Manning 1944	500	11	2.2
TOTAL	7,763	125	1.6

Method

The present study is but one facet of a general investigation into the significance of abnormal electrocardiograms occurring in apparently healthy people which is being conducted in the Faculty of Medicine, University of Manitoba. Of the total population under observation, the P–R interval was greater than 0.20 second in at least one electrocardiogram of 57 individuals. The analysis of data pertaining to these people forms the basis of this report. Details of the main study are to appear in a separate publication but may be described here briefly.

Beginning in 1946 attempts were made to contact ex-aircrew who were in apparently good health at the time their original electrocardiograms were taken in the Royal Canadian Air Force during World War II. Particular care was taken to locate as many as possible of those whose original electrocardiograms were abnormal, while those with normal tracings were included as a control. The method of contact was by letter and the periodic re-examinations planned at 5 year intervals were carried out by

physicians and hospitals throughout Canada, the United States and abroad. At the time of writing at least two electrocardiograms, 5 years apart, have been obtained on some 3,000 persons, and 500 of them have been followed for 10 or more years.

GENERAL CHARACTERISTICS OF THE GROUP

Length of Observation Period

The length of the follow-up period was not identical in all cases because the initial examinations were spread over a number of years and the subsequent re-examinations were completed at varying intervals of time. In most instances, partial heart block was present in the initial electrocardiogram but in some it appeared after the individual entered the study. The distribution of cases by the number of years of observation is shown in Table II.

TABLE II

Distribution of Cases by the number of years under Observation.

Years	Number of Cases
5	3
6	4
7	7
8	5
9	12
10	13
11	8
12	5

The lives were traced for an average of 9 years. The shortest period was 5 years and the longest 12 years. Thirty-eight or 67 per cent were followed for 9 or more years.

These 57 persons were observed for a total of 514 life years without a death. As the expected mortality provides for at least 1 death, the experience to date suggests a normal mortality.

Age Distribution

Age was calculated to the nearest birthday. The age distributions at the time of the original and the most recent examinations are shown in Table III.

TABLE III

AGE DISTRIBUTION

AGE GROUPS	AGE AT ENTRY		PRESENT AGE	
	Number	Percent	Number	Percent
15 - 19	6	11	0	-
20 - 29	31	54	4	7
30 - 39	12	21	37	65
40 - 49	8	14	11	19
50 - 59	0	-	5	9
Total	57	100	57	100

The mean age was 28 years at the beginning and 37 years when the study was completed, the average increase being 9 years. Fifty-four per cent at the outset were in the age group 20 to 29 years while 65 per cent were between ages 30 to 39 years when last examined.

Body Build

Body build is expressed as a percentage deviation from the average weight for a given height according to a build table based on the Medico-Actuarial Mortality Investigation of 1913 (25). The distributions of body build recorded at the beginning and end of the study period are shown in Table IV.

When first examined 44 per cent were 5 to 14 per cent under and 11 per cent 5 to 14 per cent over standard build. After 9 years 24 per cent were between 5 to 14 per cent underweight and 38 per cent 5 to 14 per cent overweight. This shift in body build conforms to that observed for the control population at these ages.

Associated Clinical Findings

The medical selection of personnel for industry and the armed forces is influenced by the type of employment. Minor impairments are measured in terms of their effect upon function and longevity. If an impairment does not at the time of examination and will not in the foreseeable future interfere with performance

TABLE IV

BODY BUILD

Percent of Standard Build	EXAMINATION			
	Original		Current	
	Number	Percent	Number	Percent
<-25 to -15	5	9	3	5
<-15 to - 5	24	44	13	24
<- 5 to<+ 5	17	31	13	24
+ 5 to<+15	6	11	21	38
+15 to<+25	3	5	4	7
+25 to<+35	0	-	1	2
TOTAL	55	100	55	100

of essential duties, the individual is classed as fit. The amount and variety of acceptable disability depend upon the type of occupation and in part upon the opinion of the medical examiner. Because of the cost of training and the physiologic demands of flight, the health requirements for flying are usually more rigidly interpreted than for other occupations. They do permit however the acceptance of minor defects believed not to impair function. Clinical findings abstracted from the medical files of these people are shown in Table V.

Because of its possible etiologic importance, particular attention was paid to a past history of rheumatic fever and associated conditions. In only one instance was there a history of rheumatic fever and it occurred after the discovery of partial heart block. Eight persons had scarlet fever and one an acute streptococcal sore throat prior to the discovery of heart block, a frequency of 16 per cent. A history of scarlet fever was present in 18 per cent of a control group.

In 5 instances there was an apical systolic murmur which was classified as functional. These murmurs may not be unimportant, as some degree of heart block occurred in all electrocardiograms of 4 of these people.

Hypertension was defined as any reading in excess of 140 mm. Hg systolic and/or 90 mm. Hg diastolic. It was observed in 7 subjects but was persistent in only one.

TABLE V

ASSOCIATED CLINICAL FINDINGS

Clinical Finding	Number	Initial Examination	
		Before	After
History of Rheumatic Fever	1	-	1
History of Scarlet Fever	8	8	-
History of Streptococcal Nasopharyngitis	2	1	1
Heart Murmur Apical Systolic	5	5	-
Elevated Blood Pressure	7	3 yes------no 3 no------yes 1 yes------yes	
Papilloma of bladder	1	-	1
Diabetes	1	-	1
Severe body burn	1	-	1
Myocardial Infarction	1	-	1

During the period of observation, one person developed clinical evidence of heart disease. This senior pilot who entered the study in 1939 at age 41, had a P–R interval of 0.21 second. In 1949 at age 51, he developed an acute anterior myocardial infarction and in 1952 a similar episode affected the posterior wall of the heart. His A–V conduction was not disturbed by either event.

ELECTROCARDIOGRAPHIC FINDINGS

In any one record the P–R interval of longest duration in the 3 standard leads was selected for the purpose of this study. This usually occurred in lead II. As the A–V conduction time was observed frequently to vary from record to record in the same person, the longest and the shortest recorded P–R interval for each member of the group was tabulated. The results appear in Table VI and are shown graphically in Fig. 1.

The shortest recorded P–R interval ranged from 0.16 to 0.36 second (Fig. 1). Twenty-three or 40 per cent fell within the usually accepted normal upper limit of 0.20 second. This occurred frequently where the longest P–R interval was not grossly prolonged but was not limited to this group. If one defines the upper limit of normal as the mean plus three times its standard deviation (0.24 second based upon the data of Stewart and Manning) (20) then 52 or 91 per cent met this requirement.

TABLE VI

PROLONGED P-R INTERVAL

OCCURRENCE AND VARIABILITY

IN SERIAL RECORDS OF 57 INDIVIDUALS

Duration (second)	P-R INTERVAL					
	Longest recorded		Shortest Recorded			
			.20 Sec. or less		0.24 Sec. or less	
	Number	Percent	Number	Percent	Number	Percent
>.20 - .24	39	68	19	-	39	-
>.24 - .28	6	11	1	-	5	-
>.28 - .32	4	7	2	-	3	-
>.32 - .36	4	7	1	-	3	-
>.36 - .40	0	-	-	-	-	-
>.40 - .44	1	2	0	-	0	-
>.44	3	5	0	-	2	-
TOTAL	57	100	23	40	52	91

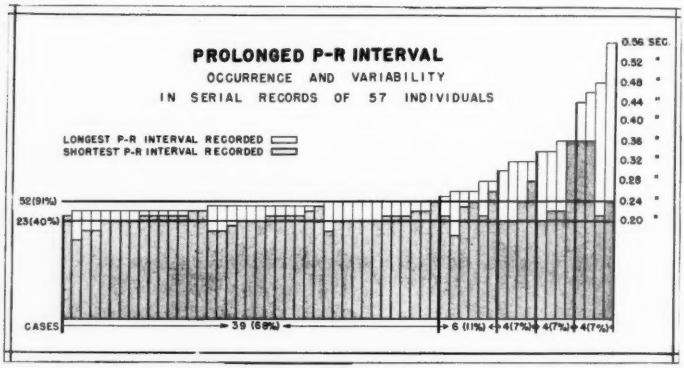

Fig. 1. The longest and shortest P–R interval recorded in the routine serial electrocardiograms of 57 people with partial heart block.

The longest recorded P–R interval ranged from 0.21 to 0.56 second (Fig. 1). Thirty-nine or 68 per cent did not exceed 0.24 second and 6 or 11 per cent were between 0.24 to 0.28 second. Four or 7 per cent each fell between 0.28 to 0.32 second and 0.32 to 0.36 second respectively. In the remaining 4 instances it exceeded 0.40 second.

Because of the known transient effect of rheumatic fever and certain other infections upon A–V conduction, one might reasonably expect to find the P–R interval prolonged on one occasion

with normal values occurring at subsequent examinations years later. Campbell (12) has remarked upon the fleeting nature of A–V block. In 46 or 82 per cent of 56* cases the P–R interval exceeded 0.20 second on two or more occasions while in only 10 or 18 per cent did it occur as a single observation. The longest P–R interval in this latter group with one exception did not exceed 0.24 second. Variations in the length of the P–R interval were noted in the serial electrocardiograms of 50 or 89 per cent of cases.

Dropped beats occurred intermittently in the electrocardiograms of 7 persons. These records usually exhibited the Wenckebach phenomenon, but occasionally missed beats occurred as an isolated finding. The longest and shortest recorded P–R intervals in these cases varied from 0.56 to 0.30 second and 0.36 to 0.20 second respectively. Dropped beats were observed only in electrocardiograms in which the longest P–R interval equalled or exceeded 0.30 second.

In addition to the routine periodic examinations, more detailed studies were possible in 13 of the 18 cases exhibiting a P–R interval greater than 0.24 second. Specific reference to selected cases permits a clearer understanding of the variability and natural course of heart block observed in this series of persons who were apparently free from heart disease.

Case 1:

On April 30, 1943, a 29 year old aircrew trainee was discovered on routine examination to have an irregular pulse. He was asymptomatic and there was no history of rheumatic or scarlet fever. Height 71½ inches; weight 150 pounds; pulse 72; blood pressure 120 - 88 mm. Hg; examination was negative and the heart size was normal by x-ray. His initial electrocardiogram is shown in Fig. 2.

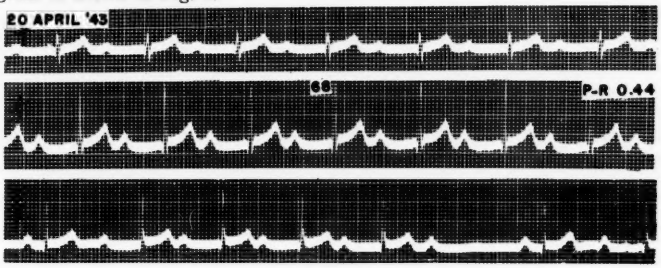

Fig. 2 (Case 1) Initial electrocardiogram 20 April 1943.

*One case omitted. He is known to be alive and well but has not consented to be re-examined.

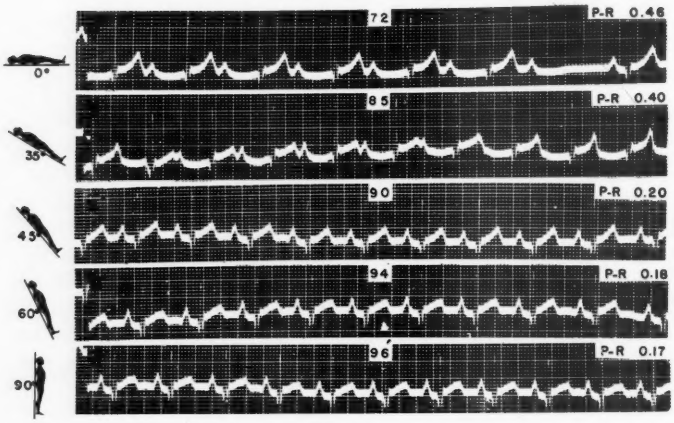

Fig. 3 (Case 1) Lead II taken at intervals during tilting from the horizontal to upright position.

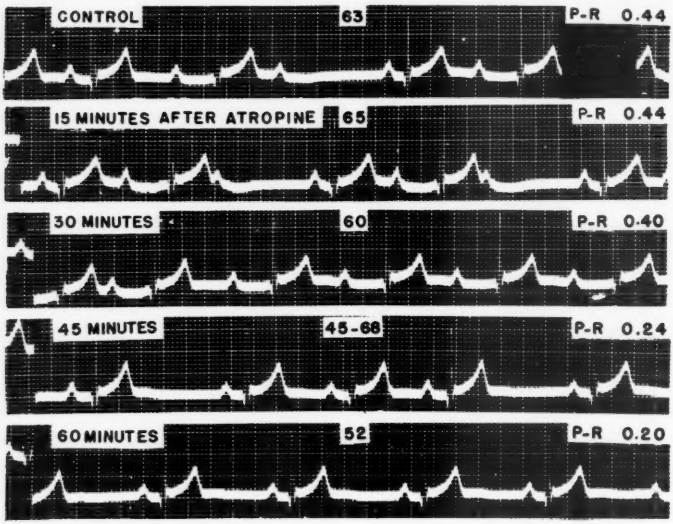

Fig. 4 (Case 1) Response to the subcutaneous injection of atropine sulphate grain 1/100.

This electrocardiogram shows a prolonged P–R interval in the 3 standard leads, measuring 0.44 second in lead II at a heart rate* of 68 beats per minute. There is a dropped beat in lead III.

Lead II recorded at intervals during tilting from horizontal to upright positions is shown in Fig. 3.

On assuming the upright position, the P–R interval is observed to decrease from 0.46 to 0.17 second. There is a coincident increase in heart rate from 72 to 96 beats per minute.

The response to the subcutaneous injection of atropine sulphate grain 1/100 recorded in lead II is shown in Fig. 4.

Sixty minutes after the injection of atropine, the pulse is regular at 52 beats per minute and the P–R interval is 0.20 second.

Lead II of his routine electrocardiograms taken between 1943 and 1952 are shown in Fig. 5.

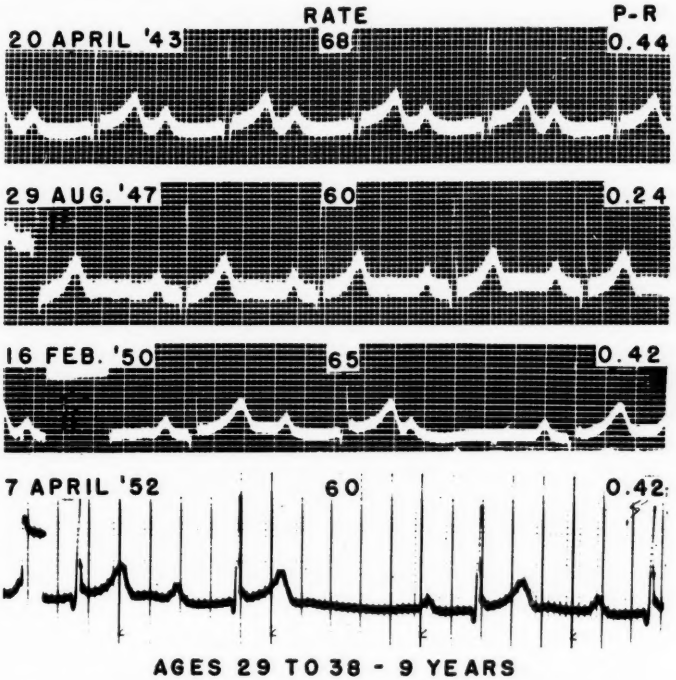

Fig. 5 (Case 1) Lead II from electrocardiograms recorded throughout the period of observation.

*Because of sinus arrhythmia, varying conduction times and missed beats, the heart rates calculated from uncut records are only approximate.

This man graduated as a navigator and was posted overseas in 1944. He became involved in an air-craft accident and was returned to Canada and discharged from the Service in 1945. He was re-examined on August 29, 1947, at the age of 32. He was then in good health and no clinical abnormalities were reported. Lead II of his electrocardiogram which appears in Fig. 5 shows a P–R interval of 0.24 second. He was next seen on February 16, 1950. The electrocardiogram shows the Wenckebach phenomenon with missed beats.

April 7, 1952, was the date of his last examination. He was employed as a salesman and felt well. Height 73 inches; weight 195 pounds; pulse 76; blood pressure 130 - 64 mm. Hg. His electrocardiogram again shows the Wenckebach phenomenon and the P–R interval varies up to 0.42 second.

Both in 1947 and 1950 the prolonged P–R interval disappeared on standing and after the injection of atropine.

This man was followed from age 29 to 38, a period of 9 years during which he enjoyed good health. The delay in A–V conduction persisted throughout, varying in degree from examination to examination. It was demonstrated repeatedly that it disappears on assuming the upright position and following the injection of atropine sulphate. This suggests that the conduction defect is due in all probability to vagal inhibition.

Similar changes in A–V conduction on standing and in response to atropine were observed in all 13 cases so tested but all did not return to normal. Usually there was an associated increase in heart rate.

Case 2:

An irregular pulse was noted on routine examination when a trained 33 year old pilot joined the R. C. A. F. on May 28, 1942. He was in good health and there was no history of rheumatic or scarlet fever. Height 67 inches; weight 138 pounds; pulse 30 - 40 irregular; blood pressure 130 - 80 mm. Hg. A soft systolic murmur was heard at the apex and in the third left interspace at the sternal margin. This murmur disappeared when the heart rate increased to 70 beats per minute and no mention of it was made on subsequent examinations. The heart was normal in size and shape by x-ray. Lead II of electrocardiograms recorded during the period of observation are shown in Fig. 6.

In his original tracing the ventricular rate is irregular at 30 to 35 beats per minute and the auricular rate is approximately 60 beats per minute. There are periods of 2 to 1 heart block and the P–R interval varies up to 0.44 second. In the record of October 10, 1944, it measures 0.24 second at a regular heart rate of 85 beats per minute while in that of October 12, 1949, it varies up to 0.34 second and there are missed beats. In the April 28, 1950, record the P–R interval is 0.32 second at a regular heart rate of 68 beats per minute.

He was last examined on May 12, 1952, and was found to be in good health. He was fully employed as the plant manager of a wood mill. Height 67½ inches; weight 150 pounds; pulse 50 irregular; blood pressure 115 - 70 mm. Hg. Apart from the irregular pulse, there were no findings referable to the heart. The electrocardiogram is similar to those recorded in 1942 and 1949.

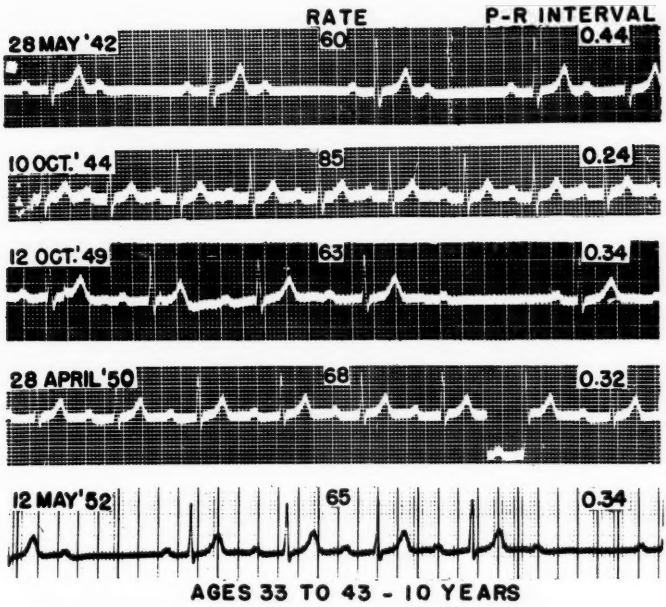

Fig. 6 (Case 2) Lead II from electrocardiograms recorded during the period of observation.

Both in 1942 and 1952 following exertion, the ventricular rate increased from 35 to 70 beats per minute and the P–R interval was reduced from 0.44 to 0.31 second and missed beats disappeared. Following the injection of atropine in 1942 and 1950 the P–R interval was reduced to 0.31 and 0.20 second respectively.

This man was followed for 10 years from age 33 to age 43 and appeared healthy at each examination. Apart from the apical systolic murmur heard on one occasion and a repeatedly irregular heart beat, there were no significant findings. The response to exertion and atropine were demonstrated repeatedly over the period of observation.

Case 3:

In compliance with an order requiring pilots age 35 and over to have periodic electrocardiograms, this 36 year old pilot was first examined on March 8, 1943. He was recovering from an acute respiratory infection but was otherwise in good health. Height 75 inches; weight 173 pounds; pulse 84; blood pressure 122 - 86 mm. Hg. His various electrocardiograms are shown in Fig. 7.

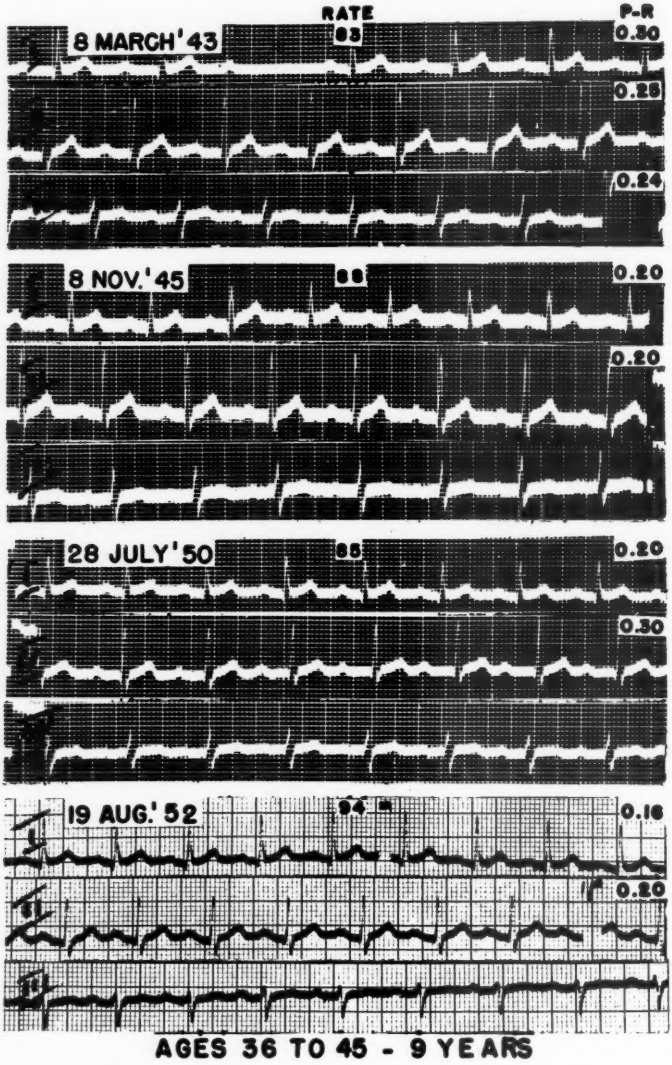

Fig. 7 (Case 3) Standard limb leads recorded during the period of observation.

In the electrocardiogram of March 8, 1943, the P–R interval is labile, measuring 0.30 second in lead I and 0.25 second in lead II. There is a dropped beat in lead I. The P–R interval recorded on November 8, 1945, measures 0.20 second in both leads I and II, and the heart rate is 88. The tracing of July 28, 1950, is of interest because the A–V conduction measures 0.30 second only in lead II.

He was last examined on August 19, 1952. His health was good and he was fully employed. Height 75½ inches; weight 214 pounds; pulse 100; blood pressure 120 - 90 mm. Hg. Clinical examination was negative. His electrocardiogram shows a P–R interval of 0.20 second at a heart rate of 94 beats per minute.

This pilot was followed from ages 36 to 45, a period of 9 years during which period he showed no evidence of disease. The transient nature of partial heart block in this individual is clearly demonstrated. The P–R interval in the original record was 0.30 second and there were dropped beats. The tracing 2 years later showed normal conduction time. At the 7th year, partial heart block was observed in only one lead (lead II — 1950). Re-examination in the 9th year again showed a normal conduction time. The shortest P–R interval occurred at the fastest heart rate.

Case 4:

Attention was directed to this 30 year old aircrew trainee on December 30, 1942, because an irregular pulse was found on routine examination. He felt well and clinical examination was negative. There was no history of rheumatic or scarlet fever. Height 68 inches; weight 155 pounds; pulse 72; blood pressure 116 - 78 mm. Hg. His original electrocardiogram is shown in Fig. 8.

This record shows a regular heart rate of 75 beats per minute and a P–R interval of 0.48 second. In some complexes the P wave is buried in the preceding T wave.

In spite of apparent good health, because of partial heart block he was hospitalized as a rheumatic fever suspect. The continued presence of normal clinical findings, including temperature, blood count and blood sedimentation rate, resulted in his release from hospital after 3 weeks.

Using lead I the A–V conduction response to atropine, changing body position and pressure on the eyeball is shown in Fig. 9.

In Fig. 9 the P–R interval before the subcutaneous injection of atropine sulphate grain 1/50, measures 0.51 second at a heart rate of 72 beats per minute. Fifty-five minutes later it is 0.20 second and the heart rate has increased to 80 beats per minute. The P–R interval on standing is seen to be 0.16 second in contrast to 0.52 second in the lying position. Dropped beats were not observed in the many feet of tracing taken on this man. As attention was first drawn to this case because of an irregular pulse, no doubt dropped beats occurred but they were not recorded. Temporary ventricular standstill was produced by pressure on the eyeball (Fig. 9).

The last examination was completed on August 28, 1950. He was in good health and there were no clinical findings. Height 69 inches; weight 170 pounds; pulse 84; blood pressure 128 - 72 mm. Hg; heart normal size by x-ray. His electrocardiogram (Fig. 8) shows P–R interval 0.21 second with a regular heart rate of 88 beats per minute. It would be of interest to observe his conduction time at a slower heart rate.

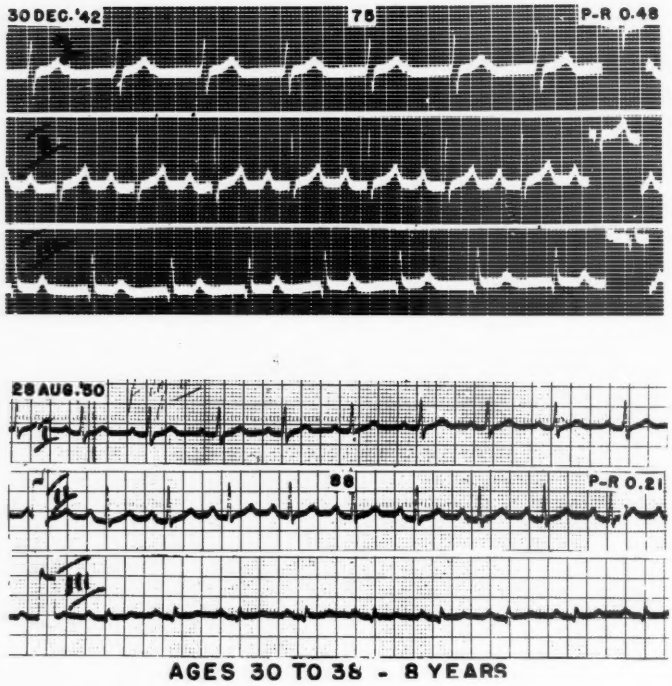

Fig. 8 (Case 4) Electrocardiograms recorded in 1942 and 1950.

This man, a stock broker, was followed from age 30 to 38, a period of 8 years, and was reported to be in good health at each examination. In spite of a marked delay in A–V conduction, missed beats were not recorded at any examination. It is of interest that he was hospitalized as a rheumatic fever suspect because of a prolonged P–R interval.

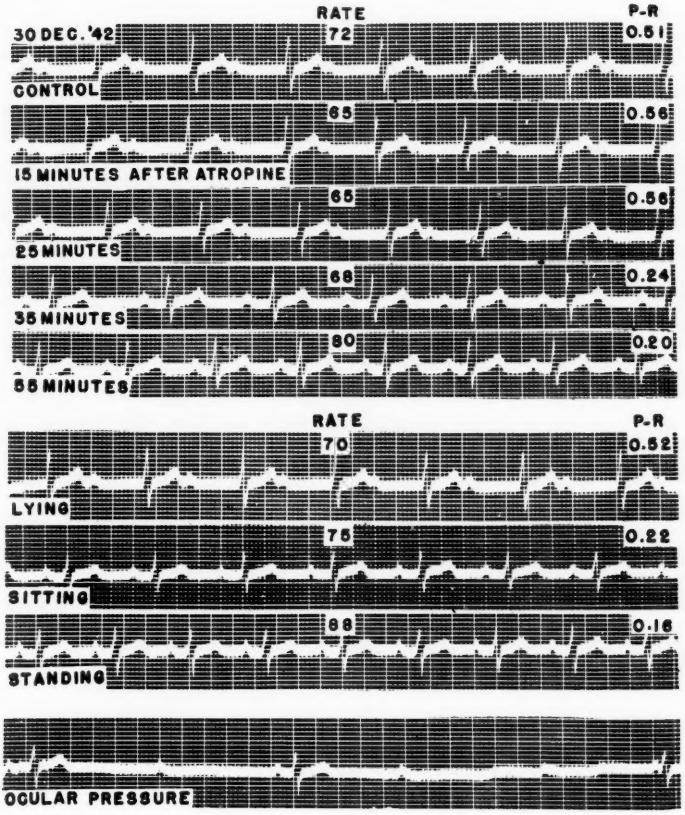

Fig. 9 (Case 4) Lead I — response to atropine, changing body position and ocular pressure.

Case 5:

On November 11, 1942, a 25 year old aircrew trainee was referred for further investigation because of a slow pulse detected on routine examination. He was in good health. There was a past history of scarlet fever at age 9 and diphtheria at age 10. Following this his activity had been restricted for 1 year. He had had repeated sore throats in childhood. Height 69½ inches; weight 162 pounds; pulse 78; blood pressure 132 - 82 mm. Hg. Nothing of significance was noted on examination. Lead II of his electrocardiograms are shown in Fig. 10.

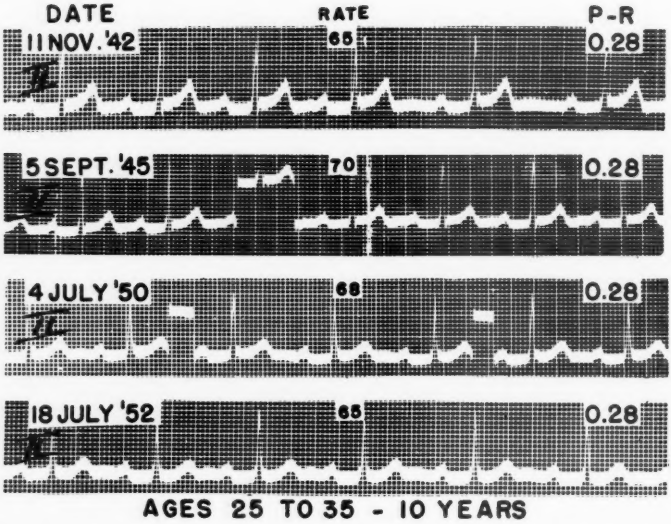

Fig. 10 (Case 5) Lead II of electrocardiograms recorded during period of observation.

His original electrocardiogram shows a P–R interval 0.28 second at a heart rate of 65 beats per minute. The records of September 5, 1945, July 4, 1950, and July 18, 1952, also show P–R interval of 0.28 second with only slight variations in heart rate.

The response to the subcutaneous injection of an unstated dose of atropine sulphate and on assuming the upright position are shown in Fig. 11.

The P–R interval 60 minutes after atropine measures 0.23 second in contrast to the control reading of 0.26 second. The heart rate is not appreciably increased. The P–R interval in the supine position measures 0.25 second at a heart rate of 71 beats per minute. On standing the heart rate is increased to 94 beats per minute and the P–R interval contracts to 0.22 second.

His most recent examination was carried out on July 18, 1952. There were no reported symptoms and the examination was clear. Height 69½ inches; weight 175 pounds; pulse 72; blood pressure 120 - 65 mm. Hg.

This man was followed from age 25 to 35, a period of 10 years. He was in apparent good health and employed as a bus driver. The relative stability of the A–V conduction defect in all routine electrocardiograms taken over the period of observation suggests the possibility that there may be some structural change in the conducting mechanism. Both atropine and assuming the erect

position shortened the P–R interval, yet in neither instance did it reach normal values. This suggests that the vagal inhibitory mechanism is active in the presence of organic block.

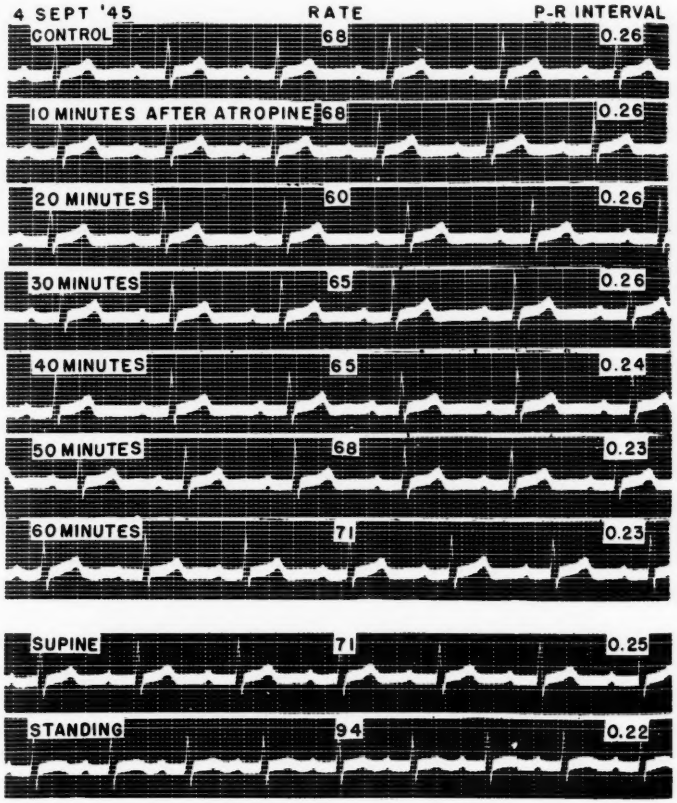

Fig. 11 (Case 5) A–V conduction following the injection of atropine and on assuming the upright position.

Case 6:

A 37 year old pilot had his first routine electrocardiogram taken on March 12, 1945. He was reported to be in good health and there was no history of rheumatic or scarlet fever. Height 74 inches; weight 176 pounds; pulse 72; blood pressure 125 - 80 mm. Hg. Clinical examination was negative. His electrocardiograms are shown in Fig. 12.

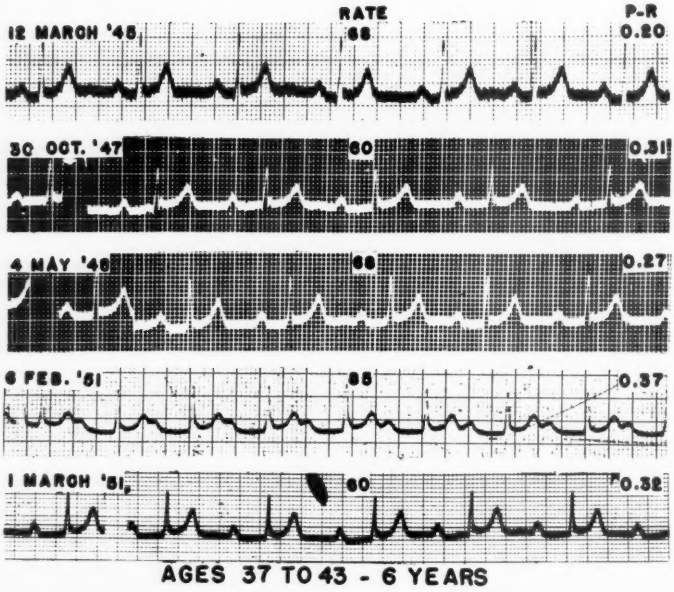

Fig. 12 (Case 6) Lead II of routine electrocardiograms recorded during period of observation.

The P–R interval in his original tracing measures 0.20 second in lead II at a regular heart rate of 68 beats per minute. His next periodic examination was carried out on February 6, 1951. He felt well and again the clinical examination was clear. His electrocardiogram shows a P–R interval of 0.37 second at a heart rate of 85 beats per minute. On inquiry it was discovered that he had consulted a physician on October 30, 1947, because of nervousness and palpitation and was rechecked by the same physician on May 4, 1948, although at that time he was asymptomatic. Copies of these electrocardiograms which appear in Fig. 12 show a P–R interval of 0.31 second in 1947 and 0.27 second in 1948.

At his last examination on March 1, 1951, he had no complaints. Height 74½ inches; weight 180 pounds; pulse 60; blood pressure 132 - 92 mm. Hg. Heart was of normal size by x-ray. Blood count normal; blood sedimentation rate 0 mm. in 1 hour (Westergren). The P–R interval of this electrocardiogram measures 0.32 second at a heart rate of 60 beats per minute.

On assuming the upright position, the P–R interval decreased from 0.32 second at a heart rate of 60 beats per minute to 0.27 second at a heart rate of 94 beats per minute. At the sixth minute after the intravenous injection of atropine sulphate grain 1/50, the heart rate was 153 beats per minute and the P–R interval measured 0.22 second from a control reading of 0.32 second. At the 15th minute, nodal rhythm appeared.

This pilot was under observation from age 37 to age 43, a period of 6 years. At some time prior to October 30, 1947, he developed partial heart block which persisted at all subsequent examinations. The P–R interval on assuming the erect position and following vagal block, decreased in duration but not to normal. In each instance there was a marked increase in heart rate. Like Case 5, the stability of the heart block suggests structural damage to the conducting mechanism. The presence of co-existing vagal inhibition was demonstrated.

Apart from the pilot who developed the classic picture of acute myocardial infarction, there were only 2 cases in which electrocardiographic changes occurred in addition to partial heart block.

Case 7:

A 24 year old pilot had his original electrocardiogram taken on April 11, 1945, when being released from the R. C. A. F. He was in good health and there were no significant findings on examination. There was no history of rheumatic fever or scarlet fever. Height 69 inches; weight 145 pounds; pulse 74; blood pressure 120 - 88 mm. Hg. The electrocardiograms taken on April 11, 1945, and June 30, 1950, are shown in Fig. 13.

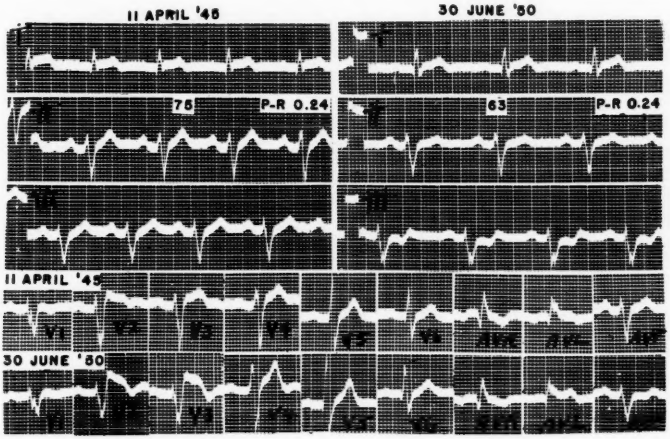

Fig. 13 (Case 7) Electrocardiograms taken April 11, 1945, and June 30, 1950.

In the tracing of April 11, 1945, in addition to a P–R interval of 0.24 second, there is an intraventricular conduction defect. The QRS duration in lead II measures 0.13 second. There are minimal Q and S waves in lead I and the precordial profile suggests right bundle branch block.

In Fig. 14 are shown lead II of electrocardiograms recorded on various occasions over the study period.

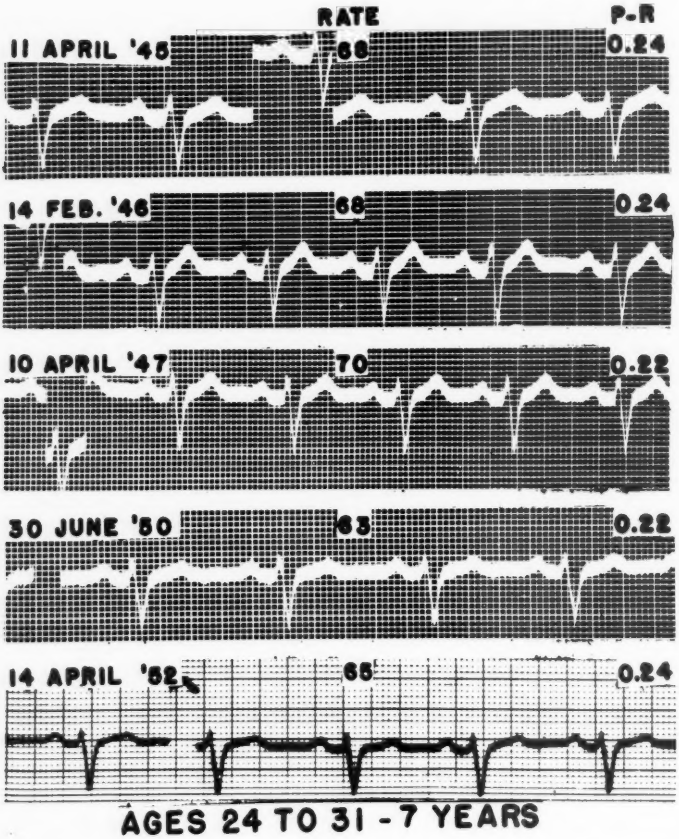

Fig. 14 (Case 7) Lead II of routine electrocardiograms taken between 1945 to 1952.

Electrocardiograms recorded in 1946 and 1947 were identical with that of 1945, the P–R intervals measuring 0.24 to 0.22 second respectively. He was next seen June 30, 1950, at which time there was no change in his clinical picture but the electrocardiogram which appears in Fig. 13 shows certain differences. The S waves in lead I are now deeper, RS–T segments in lead III are depressed and in leads V_2 and V_3 are elevated.

His last examination was on April 14, 1952. He was in good health and was employed as an aero-engine mechanic. There were no positive findings on examination. Height 69 inches; weight 150 pounds; pulse 65; blood pressure 130 - 88 mm. Hg.

The response to the intravenous injection of atropine sulphate grain 1/50 is shown in Fig. 15.

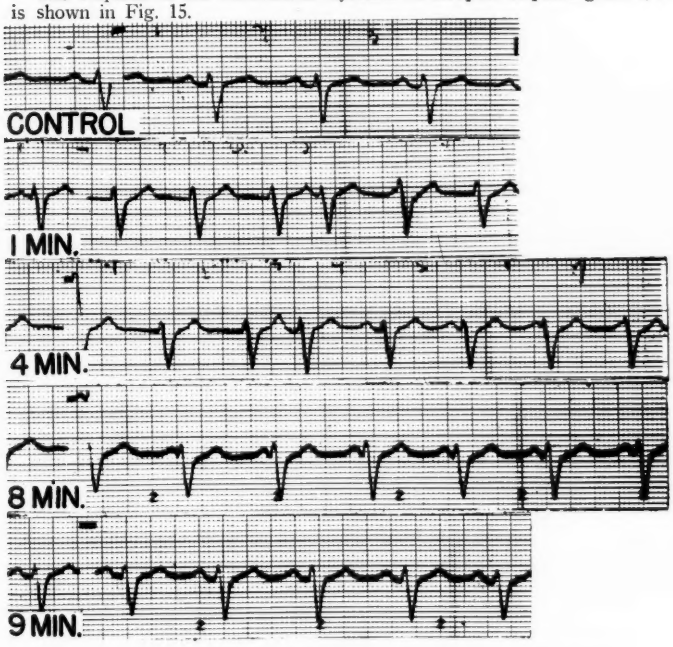

Fig. 15 (Case 7) Response to atropine.

In the record taken 1 minute after the intravenous injection of atropine sulphate grain 1/50, nodal rhythm is present at a heart rate of 92 beats per minute. There are occasional auricular premature beats. At the fourth minute, following one premature contraction, impulse production temporarily re-establishes itself in the S–A node but rapidly slips back to the A–V node. At the eighth minute sinus rhythm gradually returns and persists thereafter. The P–R interval after that varied from 0.21 second to 0.26 second at a heart rate of approximately 80 beats per minute.

This man was followed from age 24 to 31, a period of 7 years. He was re-examined on numerous occasions and at all times was found to be healthy. No heart murmurs were reported. His electrocardiograms show both an auriculoventricular and intraventricular conduction defect. Between 1947 and 1950 the form of the QRS–T complex became more aberrant. Nodal rhythm followed the injection of atropine, a finding which has been reported previously by others (4, 7).

Case 8:

A routine electrocardiogram was recorded on a 23 year old aircrew trainee on January 14, 1941. He was in good health and free from any evidence of disease. There was no history of rheumatic or scarlet fever. Height 68 inches; weight 169 pounds; pulse 84; blood pressure 150 - 88 mm. Hg and later 140 - 78 mm. Hg. Electrocardiograms taken in 1941, 1949, and 1952 are shown in Fig. 16.

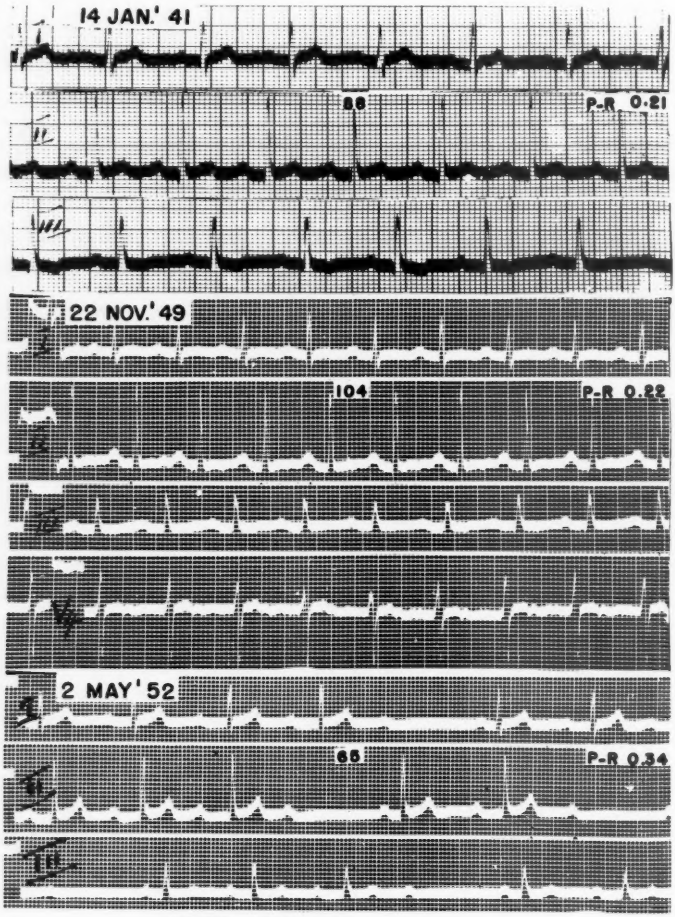

Fig. 16 (Case 8) Electrocardiograms recorded in 1941, 1949, and 1952.

In the tracing of January 14, 1941, the P–R interval in lead II measures 0.21 second at a heart rate of 88 beats per minute.

He was next examined on November 22, 1949, and was reported to be in good health. His weight had increased some 32 pounds to 201 pounds and his blood pressure was stated to be 140 - 85 mm. Hg. The electrocardiogram taken at this time shows a P–R interval of 0.22 second in lead II with a heart rate of 104 beats per minute. The T waves exhibit low voltage in the standard leads and in V_4 they are low and diaphasic.

On May 2, 1952, he underwent further examination at our request. He felt well. His weight had dropped to 189 pounds and the examiner reported a faint mid-systolic apical murmur which was not affected by exercise. Blood pressure was 140 - 88 mm. Hg. His electrocardiogram shows a P–R interval of 0.34 second in lead II and there are missed beats, the heart rate being approximately 65 beats per minute.

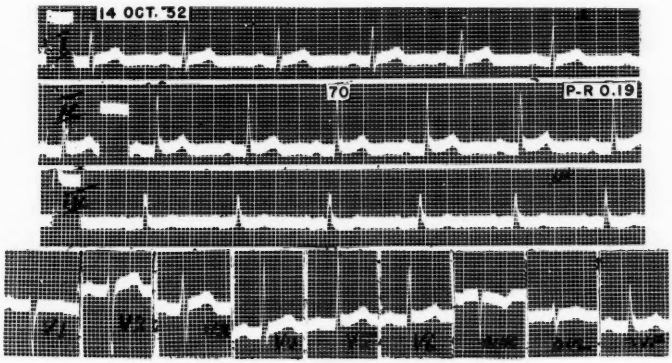

Fig. 17 (Case 8) Electrocardiogram October 14, 1952.

He was examined last on October 14, 1952, and was again said to be feeling well. He was employed in the R. C. A. F. on ground duties. The blood pressure was 150 - 100 mm. Hg and the blood sedimentation rate 6 mm. 1 hour. His complete electrocardiogram which appears in Fig. 17 shows P–R interval in lead II of 0.20 second at a heart rate of approximately 68 beats per minute. It is well within normal limits.

This man was followed from age 23 to 35, a period of 11 years calculated to the nearest birthday. A systolic apical murmur was reported on one occasion and his blood pressure showed some recent increase. Apart from this, there was no evidence of disease. Low voltage T waves were observed only in the record of November 22, 1949. The A–V conduction time which was originally 0.21 second was markedly increased in the record of May 2, 1952. On October 14, 1952, his electrocardiogram was normal. The above

electrocardiographic changes occurred while this man was in apparent good health. No explanation for this sequence of events is suggested.

Examples have been shown where following both the injection of atropine and on assuming the upright position from the supine there was shortening of the P–R interval and an increase in the heart rate. This was clearly demonstrated in Cases 1, 4, 5 and 7 (Figs. 3, 4, 9, 11, 15) and it occurred spontaneously in Case 3 (Fig. 7) in routine tracings recorded many years apart. It was also observed in other cases in this study, the details of which have not been presented. Similar changes have been reported in persons with known heart disease (12, 26, 27, 28, 29, 30, 31, 32, 33). The explanation that this response is brought about through the removal of vagal inhibition is consistent with present physiologic concepts. Atropine by blocking the vagal terminals at both the sino-auricular and auriculo-ventricular nodes, on the one hand, accelerates the rate of impulse production in the S–A node, thus increasing the heart rate, and, on the other, facilitates the passage of the impulse through the A–V node, thereby reducing the length of the P–R interval. These two functions do not necessarily act together nor are they operative to the same degree in the same person. The fact that the P–R interval does not necessarily vary directly with the heart rate is recognized (15, 31). On comparing the heart rate accompanying the longest and shortest P–R intervals recorded over the period of observation for each individual, there were only 26 instances out of 55* where the fastest heart rate occurred at the time of the shortest P–R interval. In 16 instances the P–R interval varied inversely with the heart rate. Case 9 is included to show an unusual association of heart rate to the length of A–V conduction.

Case 9:

On February 23, 1942, a 19 year old aircrew trainee was found to have an irregular heart beat on routine examination. He was in good health and there were no significant findings except for a history of scarlet fever at age 7. Height 68¼ inches; weight 150 pounds; pulse approximately 60 irregular; blood pressure 130 - 84 mm. Hg. Lead II of his routine electrocardiograms taken over the study period are shown in Fig. 18.

*Omitted case 9 and one case known to be alive but re-examination not completed.

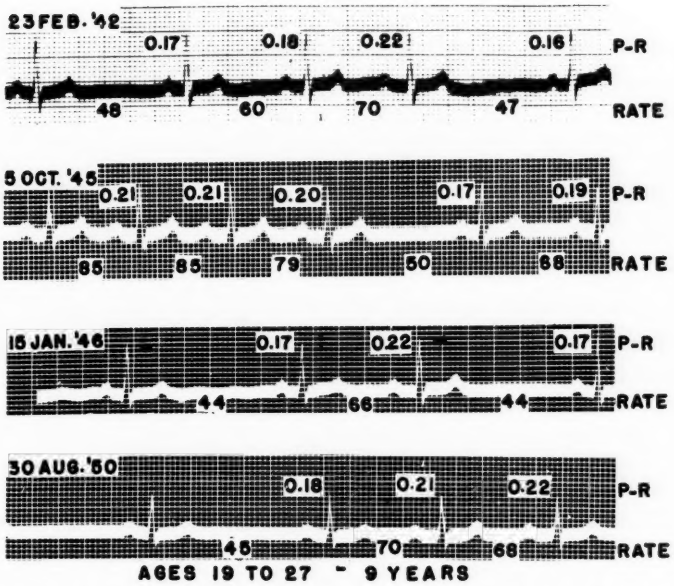

Fig. 18 (Case 9) Lead II of routine electrocardiograms taken between 1942 and 1950.

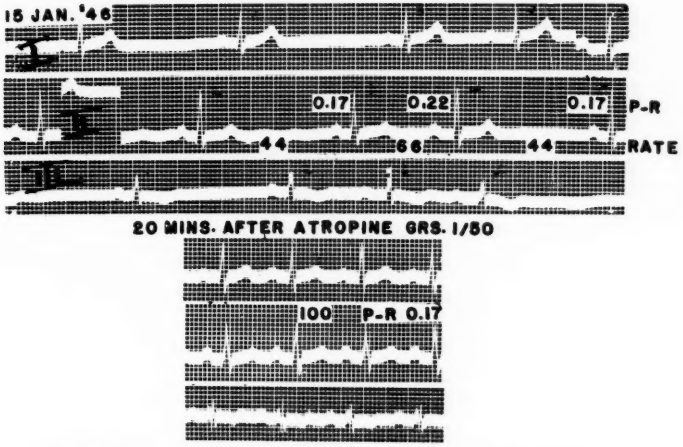

Fig. 19 (Case 9) The effect of atropine upon A–V conduction.

The tracings recorded on four different occasions between 1942 and 1950 show the heart to be beating at two distinct rates. At rates below 50 beats per minute the P–R interval measures between 0.16 to 0.18 second. At rates above 50 beats per minute, it varies between 0.18 to 0.22 second. The P waves are essentially similar in shape, indicating a constant site of impulse production in the sino-auricular node.

The response to the injection of atropine sulphate grain 1/50 is shown in Fig. 19.

Twenty minutes after the intravenous injection of atropine the heart rate is increased to 100 beats per minute and the P–R interval measures 0.17 second.

This pilot was last examined on August 30, 1950. He was reported to be in good health and there were no significant findings on examination. During the war he received severe body burns as a result of an aircraft accident. Height 70 inches; weight 164 pounds; pulse 40 - 70 irregular; blood pressure 130 - 70 mm. Hg.

This man was followed from ages 19 to 27, a period of 9 years calculated to the nearest birthday. He showed no evidence of heart disease. The duration of the P–R interval is related to the length of the diastolic pause. At the faster heart rates, the conducting mechanism is still partially refractory. The fact that it disappears with vagal blocking suggests the site of action is likely in the A–V node.

DISCUSSION

Fifty-seven apparently healthy people with partial heart block were examined and electrocardiograms recorded at varying intervals over an average period of 9 years. Apart from an irregularity of the heart rate in those with dropped beats, a delay in A–V conduction was not suspected until the electrocardiograms were examined. Electrocardiographically the observed heart block exhibited no characteristic which would enable one to identify it from heart block occurring in association with known heart disease. There were no deaths in the group which suggests a normal mortality. One person developed a myocardial infarction; heart disease was not otherwise reported.

It was not possible from the examination of any one electrocardiogram to predict the characteristics of A–V conduction in subsequent tracings of the same individual. It might shift from normal to gross prolongation of the P–R interval with dropped beats, varying degrees of block appearing for no apparent reason. Because of this marked variability and the continued absence of disease, any assessment of the clinical significance of partial heart block based upon the duration of the P–R interval would be un-

reliable. At times the degree of block varied directly with the heart rate but this relationship was not constant.

No evidence was developed to explain the etiology of heart block in these people. On a functional basis, vagal inhibition was a factor and particularly was it important in those cases where blocking of the vagus resulted in a normal P–R interval. In selected cases, the block was more stable, but even here some degree of vagal influence was usually demonstrable. Such cases suggest the probability of structural change in the conducting pathways at some site other than the A–V node where the vagal fibers terminate. Residual scars, the result of undiagnosed rheumatic fever or associated infections, minor congenital defects and degenerative changes involving the common bundle are possibilities to be considered. No explanation is offered for the hypersensitive vagal mechanism which in some people was demonstrated to persist throughout the years.

CONCLUSIONS

1. In the electrocardiograms of 57 apparently healthy people with partial heart block observed over an average period of 9 years, the longest recorded P–R intervals ranged from 0.21 to 0.24 second in 68 per cent of cases and from 0.25 to 0.56 second in the remaining 32 per cent. On at least one occasion during the follow-up period, the electrocardiograms of 40 per cent of these people showed a P–R interval not greater than 0.20 second and in 91 per cent it did not exceed 0.24 second.
2. In 82 per cent of cases, the P–R interval exceeded 0.20 second on two or more occasions while in 18 per cent it occurred as a single observation.
3. Variations in the length of the P–R interval were noted in the serial electrocardiograms of 89 per cent of cases and in only 11 per cent was the same measurement observed in all tracings.
4. There were no deaths and the evidence to date suggests a normal mortality.
5. With one exception, no person developed clinically detectable heart disease.
6. The marked variability in A–V conduction from examination to examination indicates the unreliability of using the duration of the P–R interval as an index of clinical significance.

ACKNOWLEDGMENTS

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The Royal Canadian Air Force was of invaluable assistance in providing equipment and personnel and by making available facilities for carrying out examinations at conveniently located installations.

The cooperation of all members of this group who have so willingly submitted to repeated examinations and the assistance of hospitals and physicians who have carried out the necessary examinations free of charge or at nominal fees is gratefully acknowledged.

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PRESIDENT LEE — Thank you, Dr. Mathewson, for your excellent presentation of a problem which confronts us daily. On this fine paper there must be questions that some of you would like to ask, and I know our speaker would be willing to answer them.

DR. HARRY E. UNGERLEIDER — Dr. Mathewson has presented two interesting observations upon which I would like to make some comment — one is that the pulse is a most important consideration in the evaluation of the P–R interval. A long P–R interval with a rapid pulse is pathological. For example, if you encounter a case in which the pulse rate is in excess of 90 and you have a P–R interval over .20, you are not dealing with the type of case that Dr. Mathewson is talking about today, and that fact cannot be overemphasized. Second, I would like to make a few remarks regarding the use of atropine and its effect on the P–R interval. In the presence of a rapid pulse and a prolonged P–R interval, that is over .20, the administration of atropine may result in a shortening of the P–R interval. That does not mean you have removed this particular case from the pathologic group. I have seen the P–R interval shortened to normal limits by the administration of atropine in active rheumatic fever cases over and over again. Certainly this procedure had no effect on the cardiac status.

The criteria for considering this impairment for selection should be the rate of the pulse and the degree of prolongation of the P–R interval. Now, as to dropped beats, I do not concur with Dr. Mathewson that they are entirely benign. Personally I do not like dropped beats and I believe that most cardiologists will agree with me that this condition is not normal.

Many of the cases that Dr. Mathewson presents are healthy at the moment but that is no guarantee that they will attain normal longevity. We too have had cases with dropped beats and unfortunately we have had several early deaths.

So, in summary, if you have a slow pulse you can tolerate a prolonged P–R interval in young people, but after age 40 I think you had better exercise your underwriting judgment, because such cases may or may not be on a pathologic basis. Weigh your dropped-beat cases very carefully and, finally, do not be deceived by the atropine test.

DR. MATHEWSON — I agree with Dr. Ungerleider's comment about atropine. The fact that partial heart block disappears following the injection of atropine does not necessarily establish its innocence. This fact has been reported by different observers particularly with reference to rheumatic fever. I feel a little more liberal than he does about dropped beats. It is only a matter of degree. If a person is under age 40 and there is no clinical evidence of disease, I think the risk is probably a standard one. On the other hand in an older person entering the period of degenerative disease, one must be more cautious.

Undoubtedly these cases I showed today have a varied etiological background and perhaps time will tell us which ones are significant and which ones are not. I think it is true that in any clinical assessment where thorough investigation fails to show corroborative evidence of disease, a single unusual finding may be treated liberally, be it albumin in the urine or a prolonged P–R interval.

PRESIDENT LEE — Thank you very much, Dr. Mathewson.

Our next speaker will be Dr. Ralph M. Filson whose subject is "The Business of Insurance and the Profession of Medicine." We felt it was timely to have some groundwork laid here on this subject — something that might be used in the future for further expansion and for publication in the medical journals. We assigned the problem to Dr. Filson because, as you who have worked with him know, his work is thorough. He needs no introduction, and we are happy to have him with us. Dr. Filson.

THE BUSINESS OF INSURANCE AND THE PROFESSION OF MEDICINE

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The existence of this Association of Life Insurance Medical Directors, its size, and the character of its membership as measured in terms of those quality standards which apply within the medical profession spell proof that the business of insurance and the profession of medicine have communities of interest. They suggest also that within these communities there may well be areas deserving specific degrees of careful inspection and review in efforts to focus attention upon the magnitude of some of the foundations upon which our inter-relationships have been builded and upon the justifications which they provide for increases in understanding and in friendly cooperation between representatives of a great business and a noble profession.

It should not be forgotten, in thoughts of this character, that there exists in the Medical Section of the American Life Convention another medical body of distinction whose membership is drawn from the ranks of doctors specializing in insurance medicine. Medical directors and the memberships of their departments from 205 insurance companies make up the Association of Life Insurance Medical Directors of America. There are 231 companies with medical department membership in the American Life Convention. A majority have memberships in both of these organizations so that in combination they represent a grand total of 283 insurance companies. Probably the names of both of these Associations may create erroneous reactions on the part of our colleagues in private practice as well as by others outside the insurance business who may conclude from these names that the ranges of our interests are limited to Life Insurance. There could be an implication that this line represented the only field of insurance in which the medical profession functioned as an integral part, or within which situations occurred through

which the business of insurance came into working relationships with medical men in private practice.

We know, as others may fail to recognize, that today in ever increasing numbers our companies are active in fields of protection beyond those of Life Insurance. Historical records disclose ever broadening and multiplying situations in which the need for medical care and occasions requiring financial assistance in meeting the costs of that care have been recognized and dealt with through the medium of insurance. If life insurance were the only item with which we were concerned, my discussion of the segment of those relationships with which I propose to deal within the title of this paper would be a limited one. It would consist of the presentation and brief discussion of a comparatively short series of figures. I have a broader purpose than this, with my objective being one of reviewing as fully and as factually as possible the sources and the amounts of money now being distributed each year, through channels of insurance, to physicians in private practice in this country. I propose to consider payments which are made directly in respect of practicing physicians' services as rendered to companies by regularly or specially appointed medical examiners and by attending physicians whose patients become insurance applicants. I shall also include in these considerations those amounts disbursed by virtue of charges which are made by physicians for their services to patients who are insured individuals.

As a preliminary to these undertakings, it is essential that our recollections of historical developments be refreshed as regards the various lines of insurance coverage productive of payments to doctors in private practice. The beginnings of life insurance in this country, in significant amounts and general distribution, can really be placed as occurring about midway in the nineteenth century. Earlier small scale experimentation had been neither stable nor successful and was not given any worthwhile public recognition. Between 1840 and 1850, however, the need for formal applications for insurance and for medical selection in connection therewith had been accepted. These fundamentals in their continuance have been strengthened and the technics through which they function have been improved throughout the years which have followed. (1)

Although some limited types of sickness insurance had been written and were available concurrently with earlier undertakings in the life insurance field, it was not until 1864, when insurance against accidental injuries made its appearance, that sickness insurance commenced to be a real mechanism of protection. Subsequently, these two lines have been very closely related, both as regards companies providing them and in their administration. They have been lines written by both life and casualty companies, since they do lend themselves in these regards to differing concepts and methods of operation. (2)

Initially, and for a good many years, accident and sickness insurance had as its chief function indemnification of policyholders for losses of earning capacity as a result of either illness or bodily injury, with accident policies having provision for principal sum payments when losses of life or of members were caused by accidental injuries.

The association with the business of insurance by members of the medical profession who were in private practice during this era was limited to their acting on behalf of companies in the roles of regularly appointed medical examiners. This association thus was not a general one. Insofar as monetary returns were concerned, they consisted only of fee payments to those who were examiners and who were called upon to make medical examinations of either applicants for insurance or of claimants.

From the practical point of view of our aims this morning, it can be said that concepts of the purposes and methods of insurance, as these were related to losses of time, limb, or life, changed little during the second half of the nineteenth century. Broadened and more varied protections against the contingencies of modern living have come into the insurance picture largely since the turn of the century. In 1910, workmen's compensation insurance, as we know it, had its origin. (2) At about the same time, group insurance, originally on a life basis and later on an accident and sickness basis, made its appearance. (3) Probably because of features which were a part of workmen's compensation, attention became focused upon insurable exposures beyond those of losses of life, limb, or time. There was a recognition that losses of money dependent upon medical and hospital care

represented substantial drains upon the resources of those who were disabled. Thus, as early as 1922, hospitalization coverage was first written, and in 1927 a medical reimbursement feature to cover any and all costs of hospital, nursing, and physicians' care up to specified maximum amounts became incorporated in the accident policies of many companies. (2) This latter mentioned date was only 25 years ago and in the intervening quarter of a century, on both individual and group bases, there has been a continuing expansion in types of protection which have been made available, through insurance channels, against the costs of practically every item of medical care required in connection with the influences of disease or injury. Among these protections may be enumerated hospital bed and board, nursing care, miscellaneous hospital services, laboratory procedures, surgical operations, and office, home and hospital visits by physicians.

It is apparent that with the modern expansion and growth of fields within which insurance functions and which involve patient-physician relationships, there has of necessity been developing ever larger areas where there are grounds for clearer understandings and fuller cooperation between the insurance business and the profession of medicine as represented by those physicians who are in private practice. There are many mutualities of interest between our business and our profession. The business has been endeavoring and will continue to endeavor to exercise its best efforts to meet public need and demand for a practical solution of the problem of providing sound media for prepaying through the allocation of regular small amounts in the nature of insurance premiums, against those costs of medical care which, when they strike an individual or family, may assume proportions of disaster. The medical profession, with increasing numbers of our citizens so protected, will have assurance of payments for services which, while not always as large as they may think is deserved, will nonetheless be sure.

Complaints are sometimes registered by doctors because of the time which is consumed in the completion of lengthy and complex forms as proofs of claim for insurance companies. This type of complaint has in too many instances been a legitimate one. Its cause can be largely eliminated. Efforts to that end are continuously being made within the ranks of those in the insurance busi-

ness who are charged with claim administration. The completion of proofs will eventually, if it does not now, represent a no greater burden than the followup in bookkeeping and accounting associated with receipts, on the part of doctors, of piecemeal payments for services rendered, or no payments at all.

An indication of degrees of public response to the availability, at reasonable rates, of these more modern forms of insurance protection is to be found in figures assembled and presented in its annual reports during the last several years by the Survey Committee of the Health Insurance Council. (4) Table I which follows gives the numbers of persons in the United States covered through insurance companies for hospitalization, for surgical benefits, and for medical care benefits at the end of each of the three calendar years which are shown, with the latest of these being 1951. These figures are taken from Survey Committee reports, with an application of the factor suggested by the committee in correcting gross figures to those nets in which there have been exclusions on account of possible duplications of coverage as between group and individual contract policyholders. The section of the table representative of percentages of increase of coverage, year by year, applies only to protection expansion in these fields through the medium of insurance companies and has been developed through straightforward mathematical calculations founded upon the figures which precede the percentages in each of the divisions.

TABLE I

Type of Coverage	Number of Persons Covered Through Insurance Companies (000 Omitted)			Percentage of Increases Over Previous Year	
	1949	1950	1951	1950 over 1949	1951 over 1950
Hospitalization	29,972	37,000	44,650	23%	20%
Surgical Benefits	23,353	32,972	40,039	41%	24%
Medical Care Benefits	4,694	7,849	11,471	67%	46%

Apart from those opportunities for prepayment afforded through insurance companies, there do exist corresponding means of protection as provided by other voluntary agencies. While it does not come within the scope of this discussion to deal in any

detail with the results attendant upon their efforts, it is only fitting to observe that in the over-all of the three types of coverage which have been specified, these agencies in combination have protected an additional number of persons almost equaling the total who have their coverages through actual insurance policies or certificates. Thus, it is obvious that in the very recent past there has been a rather phenomenal and consistently increasing spread of voluntary prepayment protection against the expense of medical care, whether in or out of hospital, or whether dependent upon treatment at the hands of either surgeons or physicians. These types of protection are now held by significantly sizable numbers of our citizens not otherwise provided for in these regards. These types of instrumentalities for protection, sold at prices permitting marketability and associated with ever broadening distributions, may well represent the most desirable and the most practical method of meeting something of a challenge which has been laid down by public demand in this area of relationships and dealings between the average citizen and the average source of his medical care.

Alternative methods of dealing with this type of problem can be developed, but it is for each of us, who is best equipped to understand the deeper purposes of the business of insurance and of the profession of medicine, to determine for himself whether alternative methods, of which he may think, could more effectively and more equitably deal with those basic needs which exist. If our present approach to these matters encountered in our modern-day sphere of public relationships is as worthy and as sound as I believe it to be, then it surely deserves our honest, thoughtful and fair consideration and handling. Representatives of the business of insurance and of the profession of medicine should unite in affording these plans a reasonable and a decent trial. We should be alert to the fact that they can be destroyed through abuses, and each of us should recognize individual responsibility and obligation to ferret out and to put down those types of abuse which are the antithesis of fair play.

Having reviewed something of the development of the existing character of the insurance situation, it follows that a next logical consideration is one having to do with the physician population of the country. We should also know something concerning

average gross and net incomes from all sources on the part of members of the medical profession and especially on the part of those whose incomes are derived solely from the conduct of private practices. Figures indicative of factual information concerning those subjects during recent years are contained in Table II which follows:

TABLE II — U. S. PHYSICIANS' DATA

ITEM	TOTAL NUMBER 1951			NUMBER IN PRIVATE PRACTICE 1951		
MEMBERS OF MEDICAL PROFESSION (5)	211,680 (estimated)			152,000 (estimated)		
		NON-SALARIED				
		Mean	Median			
GROSS INCOME (6)	1949	$19,710	$16,108			
	1950					
	1951	22,298	18,169			
		ALL			NON-SALARIED	
		Mean	Median		Mean	Median
NET INCOME (6)	1949	$11,058	$ 8,835	1949	$11,744	$ 9,561
	1950	11,538	9,311	1950	12,324	10,518
	1951	12,518	10,285	1951	13,432	11,191

With those foundations in mind which have been laid in the foregoing, further factual information bearing directly upon the objective which I have set out can now be superimposed. The objective, it will be recalled, was to be concerned with but one link in the chain of associations between the insurance business and the medical profession. While this link by virtue of its pure materialism may be considered by some as deserving classification in the realm of the more sordid, it is nonetheless forged from the substance of realism, and that substance provides a means of mensuration probably not equaled by any other in actually defining the scope of our inter-relationships. It has to do with the volume of the flow of dollars running annually to those members of the medical profession who are engaged in private practice

and which comes from insurance sources, either as a result of direct service to insurance companies or direct charges to insurance policyholders.

The tables which appear below show in reasonable divisions the dollar amounts paid from companies engaged in the insurance business in this country during the calendar year 1951, within the classifications which are stated. These amounts are so directly related to practicing physicians' services and charges that they may be accurately designated as having been received by members of the medical profession in private practice, either directly or indirectly.

TABLE III

Payments to practicing physicians made directly by insurance companies for examinations and reports, either regular or special, and for statements from attending physicians. (7)

Year	Total Amount
1951	$16,000,000

TABLE IV

Payments in respect of physicians' charges to policyholders having either Group or Individual Policies providing Surgical and Medical Care Benefits. (7)

Year	Type of Insurance	Amount Paid
1951	Group Surgical & Medical	$160,000,000
1951	Individual Surgical & Medical	55,000,000

TABLE V

Payments in respect of physicians' charges to policyholders having Blanket Reimbursement under Personal Accident Policies and to those having Infantile Paralysis or Polio Policies. (7)

Year	Amount Paid
1951	$7,000,000

TABLE VI

Payments in respect of physicians' charges to policyholders pro-

tected under Workmen's Compensation and Automobile Accidental Injury Insurance. (7)

Year	Type of Insurance	Amount Paid
1951	Workmen's Compensation	$111,000,000
1951	Automobile Accidental Injury	9,000,000

TABLE VII

Summary of Tables III, IV, V and VI. (7)

Table	Amount Paid
No. III	$ 16,000,000
No. IV	215,000,000
No. V	7,000,000
No. VI	120,000,000
Total	$358,000,000

When we undertake to assess the individual sharing of those amounts in terms of averages and of percentages of gross individual incomes, the results are those which appear in Table VIII.

TABLE VIII

Distribution of annual payments from insurance companies to practicing physicians in terms of average amount per individual and percentage of gross income.

No. of Practicing Physicians	Total Amount Paid	Average Amount Per Individual	Percentage of Gross Income
152,000	$358,000,000	$2,356	13%

I conclude, on the strength of those facts which have been assembled and which represent in considerable part data not hitherto compiled, that there is established, at least in terms of dollars and cents, a startlingly substantial basis for agreement upon certain premises. 1. The business of insurance and the profession of medicine are today more than ever before joint participants in a worthy and a constructive series of causes. 2. These causes are intimately associated with the interests and welfare of ever larger segments of our general population. 3. They involve efforts having to do with the provision and the administration of practical and equitable methods of voluntary prepayment of expense to cover reasonable costs of necessary medical care. 4. The methods employed in these programs are such that they

not only meet public demands but they preserve complete freedom of physician selection on the part of the patient as well as those fundamentals of physician-patient relationships so essential to all that is good in the practice of medicine. 5. With joint participation in plans of this order, there must necessarily go joint responsibility in the elimination of those abuses which can weaken and destroy. 6. There exists a community of enterprise in our joint privileges of service to the public which should create greater efforts toward sympathetic analysis and understanding of each other's viewpoints and problems. 7. Out of such an understanding there may be an anticipation of increasing mutual advantages attainable through the exercise of a more patient and a more friendly spirit of cooperation on occasions when additional facts are sought by either party in the resolution of those comparatively infrequent situations in which final decisions must be dependent upon amplification or explanation of existing data.

Although those figures which have been presented covering direct payments going to practicing physicians from insurance sources are impressive, a discussion of the character which has been undertaken here would be incomplete if it did not include those additional observations which follow and with which I shall terminate my remarks.

In 1951, life insurance companies in this country paid to beneficiaries of deceased policyholders a total of $1,709,401,000. (8)

They paid a total of $82,000,000 in Income Disability Benefits to living but totally disabled life insurance policyholders. (7)

They paid a total of $503,161,000 on Matured Life Insurance policies to the individuals owning those policies. (8)

They paid a total of $277,042,000 in Annuities to those having made this type of insurance investment. (8)

They paid a total of $1,394,090,000 in Cash Surrender Values and Cash Dividends to living policyholders. (8)

Additional to these amounts, companies writing Accident and Health Insurance in this country paid out a total of $445,000,000 in Weekly Indemnity and Accidental Death Benefits during 1951, under Group and Individual policies in these types of coverage. (7)

These payments combined represent a distribution, within the year 1951, of a grand total of $4,410,694,000, much of which was paid either during periods of disability or at the time of death following illnesses or injuries. While there are no practical means through which there can be any accurate determination of the percentages of those moneys used in payment for physicians' services, it is, I contend, a reasonable conclusion that some proportion of these vast sums was so employed. Mention is made of this aspect of the business of insurance only for the purpose of establishing that the figures and the percentages specified in the tables which have been given and which apply to amounts known to have gone to practicing physicians do not represent the whole story. There are undoubtedly substantial additions, originating from insurance payments, going to the same recipients by way of less direct and less easily defined routes.

Since we, as medical directors, are a part of the business of insurance while at the same time being members of the profession of medicine, we may well occupy a signal position of leadership in guiding both groups. We have an opportunity to know the structure of our own products and the reasons why they exist as they do. We can employ our specialized knowledge in pleas for the strengthening of weaker areas in our programs and for the development of better means by which to administer those programs. We also have it within our power to explain to our colleagues in clinical medicine, and to defend where necessary, the objectives and the mechanics of those programs which we have helped to build. Frequently, explanation leading to better understanding is the real key to improved relationships, both professional and public.

There are, I believe, some conclusions in the fields of which we have been speaking to which we, as doctors, whether active in insurance or clinical medicine, may all subscribe. We have associated interests which ought to promote even greater degrees of mutual respect, particularly in connection with our common objectives of ever better and more available medical care to ever increasing numbers of our citizens. We should recognize that we can work more closely and understandingly in teaming up toward further progresses in joint contributions to this end. We are all concerned in promoting the acquisition, through voluntary

channels of easy thrift, of means and methods which will permit ready, reasonable and prompt payments for medical care services which become necessary.

Yes, it bears repeating — the business of insurance and the profession of medicine have strong bonds of affiliation in their respective fields of service to mankind.

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PRESIDENT LEE — This paper is indeed magnificent. We are running behind time, but I would not want to rob anyone of a question or two if there is someone who would like to ask one.

DR. CHARLES B. AHLEFELD — I think the material in this paper is too important to be buried in the archives of this Association. Serious consideration should be given to disseminating parts of it in a widespread manner in various publications if at all possible.

DR. HAROLD M. FROST — I want to extend my own personal congratulations for a wonderful presentation. I am particularly interested, of course, in the life insurance companies and the relationships between the medical departments and the practicing physicians. I have alway maintained that life insurance companies throughout the country, through the medium of their medical departments and their medical directors, cannot afford to antagonize or irritate in any way the practicing profession. Most certainly we rely on them to safely conduct the affairs of the institution of life insurance.

You spoke about certain abuses. You mentioned, for one, the blanks which physicians are required to complete. You had in mind, I suppose, not only examination blanks but attending physicians' statements. Have you in mind other abuses which you might bring to our attention?

DR. FILSON — Abuses, I think, are multiple, potentially so and factually so. They do not all exist as would be expected on either side of the related associations or organizations. They are not all insurance company abuses. They are not all practicing physicians' abuses. There are abuses certainly on both sides.

Claim forms are one of the things we have to improve upon sooner or later. Dr. Simmons' committee is working on this, and together with the International Claim Association and the Health Insurance Council, they are all greatly concerned about this question of long, complex blanks. The claim blanks are notoriously bad in many instances.

Now there are other abuses, of course. We should discuss with our colleagues in clinical medicine the real depth of purpose in these insurance programs and what they aim to accomplish, and try to establish in their minds that they ought to be treated fairly; that they should not use the fact that this medium of protection has been provided to start physicians' charges at the level where the protection leaves off. The accusation is made, and I believe with degrees of justification, that these insurance protective mechanisms are about to boost fees. Some physicians and surgeons feel that "this is gravy — what the people have in the way of insurance protection" — and fees are levied, commencing where the protection leaves off. That is an unfair attitude.

With maximum amounts available, as is true in connection with many of our individual contracts, overcharging way beyond the reasonable average fee for a given service to consume practically the entire maximum is another abuse which does exist.

These are the things that I think we as medical directors should talk over with our colleagues in clinical medicine. I believe that today to a greater extent than ever before we find among our colleagues in clinical medicine a mind receptive to serious and thoughtful discussion of this type of subject.

PRESIDENT LEE — Thank you again, Dr. Filson. There are many questions that we all would like to ask, but we just do not have the time.

We will proceed with our next paper. I was very anxious to have on this program Dr. Robert H. Williams from the University of Washington Medical School. I had not had the pleasure and the privilege of knowing Dr. Williams personally, although I knew a great deal about his background. Because of my inability to go to Seattle at the proper time, I prevailed upon an old friend and a prominent man in his own right, Dr. Edwin S. Bennett, to carry on negotiations for me. Through his kindness we are indeed fortunate in having Dr. Williams speak to us on "Syncope, Vertigo, and Dizziness." Dr. Williams.

SYNCOPE, VERTIGO, AND DIZZINESS

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Many terms are used to indicate sensations of disturbed equilibrium. Among these are dizziness, giddiness, light-headedness, swimming in the head, feeling of falling, unsteadiness, biliousness, confusion, vertigo, faintness, black-out and syncope. The connotations of these terms are variegated and vague; thus a few definitions are in order. *Dizziness* is a sensation of unsteadiness with a feeling of movement within the head. *Vertigo* is a sensation of movement or rotation in space. The individual may feel that he is rotating or falling or may feel that his environment is rotating. *Syncope* is a temporary brief suspension of consciousness, beginning and ending rather suddenly. *Collapse and shock* are closely related to syncope.

Many factors are involved in the maintenance of equilibrium, but the five most immediately concerned are: 1) eyes, 2) vestibular apparatus, 3) cerebellum, 4) proprioceptive system, and 5) cerebrum. Not only must these units be functioning, but their functions must be well coordinated.

VERTIGO

The vestibular labyrinth has as its only function equilibration. The endolymph in the three canals responds readily to changes in position of the head. Impulses from the canals traverse the vestibular portion of the 8th cranial nerve to the medulla from whence some impulses travel to the cerebellum and cerebrum and others to the eyes. Marked stimulation of the ocular fibers causes nystagmus, and of the cerebellar-cerebral fibers, vertigo. There are many diseases that may involve these vestibular tracts somewhere along their course. With hyperstimulation both nystagmus and vertigo may be produced; one of these tends to occur without the other if the lesion is in the central nervous system at a point

where the vertiginous fibers are significantly separated from the nystagmic. If the disease process destroys the fibers rather than stimulates them, neither vertigo nor nystagmus may be present, but there is a disturbance in equilibrium. Associated symptoms and signs are often of aid in localizing the disease. These are: 1) nystagmus, 2) tinnitus, 3) deafness, 4) nausea and vomiting, and 5) disorders of neuromuscular system.

The results of the Barany tests, x-rays, electroencephalograms, spinal fluid analyses, etc., are of considerable aid. The Barany caloric test is based upon the fact that sudden instillation of water at a temperature greatly contrasted with that of the body will cause the labyrinthine endolymph to expand or contract, thereby overstimulating the vestibular nerve, causing nystagmus and vertigo. However, if certain portions of the labyrinth or vestibular pathways are destroyed, the normal responses are not obtained. The knowledge of the nature and extent of disturbance in the responses to the Barany test is of considerable aid in determining the type and location of the lesion. A special effort is made to determine whether the disease is central (CNS) or peripheral (labyrinth and/or vestibular nerve). Some of the pertinent differences in manifestations are listed in Table 1.

TABLE 1

COMPARISON OF PERIPHERAL AND CENTRAL VERTIGO

PERIPHERAL	*CENTRAL*
Paroxysmal vertigo	Continuous vertigo
Minutes — hours	Hours — days
Outlasts other symptoms	Does not persist after attack
Nystagmus rotary, horizontal or mixed	Nystagmus vertical
Poor or no nystagmus on Barany test	Perverted or inverse nystagmus on Barany test
True directional rotatory vertigo	Vertigo of a vague type

Many and varied diseases may produce vertigo; some of these are: 1) blocking of a eustachian tube, 2) wax in the meatus, 3) inflammatory lesions in middle ear, 4) lesions involving vestibular division of the 8th nerve (a) Meniere's disease, (b) alcoholism,

(c) tumors, (d) trauma, (e) streptomycin, (f) allergy, 5) gross lesions of the cerebellum in which the vestibular connections or nerve are involved, and 6) acoustic neuroma.

The classification of Ford, as modified by me (Table 2) is of some aid in understanding certain aspects of the pathologic physiology associated with vertigo.

TABLE 2

GENERAL PATTERNS OF VERTIGO IN VESTIBULAR NERVE DISEASE

A. Nerve Stimulation
   1. Spontaneous — not initiated or relieved by movement
      a. Recurrent (Meniere's, chronic otitis)
         No symptoms between attacks
      b. Non-recurrent (pyogenic labyrinthitis or meningitis, syphilis, herpes, streptomycin, quinine, aspirin, allergy)
   2. Induced by sudden head movement
      Barany test — hyperreaction

B. Nerve Depression — due to anything destroying the vestibular nerve
   1. Unsteadiness, exaggerated in dark and by sudden movement
   2. Inability to fix objects with eyes
   3. Temporary with only unilateral disease
      Barany test — negative response

N.B. Incoordination of function of various equilibrating units gives symptoms similar to vestibular stimulation.

Meniere's disease is one of the most classic entities associated with vertigo. It is characterized by: 1) vertigo, 2) nystagmus, 3) nausea, 4) tinnitus, 5) nerve deafness, 6) attacks intermittent, and 7) unconsciousness occasionally.

Much needs to be elucidated relative to the etiology of Meniere's disease. Supposedly, pressure of the endolymph builds up, leading to the explosive attacks. Allergy, disturbances in water and electrolyte balance, and other factors have been incriminated. Degenerative 8th nerve changes finally develop.

Many therapies for Meniere's disease have been proposed; some of these are as follows: 1) recumbent position, 2) dramamine 50 mg. t.i.d., 3) phenobarbital or other sedation, 4) restriction of

sodium and water, 5) ammonium chloride, 2 Gm. t.i.d., 6) potassium chloride, 2 Gm. t.i.d., 7) destructive labyrinthotomy, and 8) section of vestibular portion of 8th nerve. Conservative therapy should be thoroughly tried before resorting to surgery. Destructive labyrinthotomy is preferable to neurotomy.

SYNCOPE

Most instances of syncope are due to a marked sudden decrease in the supply of blood and/or oxygen to the brain. This, in turn, may be due to, a) disease of the brain or its blood vessels, b) abnormalities in the blood components (e.g. anoxemia), c) inadequacy in the frequency or forcefulness of the heart beat, or d) inadequate return of blood to the heart, as in peripheral vasodilatation or loss of blood volume.

Some of the conditions that cause syncope by promoting peripheral vasodilatation are listed in Table 3. Ordinary fainting is a

TABLE 3

FACTORS CAUSING SYNCOPE BY PROMOTING PERIPHERAL VASODILATATION

1. Psychogenic fainting
2. Pain (gonadal, solar plexus)
3. Orthostatic
4. Carotid sinus — peripheral type
5. Post-sympathectomy
6. Vasodilator drugs
7. Tissue damage
8. Bacterial toxins
9. Anaphylaxis
10. Physical exhaustion
11. Debility
12. Prolonged rest and recumbency
13. Addison's disease
14. Hypotension
15. Overheating

good example of this mechanism. A woman on receiving a startling telegram may suddenly become markedly pale and fall to the floor

unconscious. The veins are collapsed, the skin is cool and moist and the pupils dilated. The severe emotional reaction was associated with dilatation of the blood vessels, particularly those in the splanchnic region. A sympathetic reaction is associated with the fainting. The fall leads to a horizontal position, permitting rapid return of blood to the head. If the subject does not soon acquire the horizontal position, a convulsion may ensue, the muscular contractions forcing the blood back to the heart and thence to the brain, thereby aiding in the resumption of consciousness. Sudden severe pain, particularly in the solar plexus or testes, may produce syncope as a result of the peripheral vasodilatation. There are a number of other instances where reflex vasodilatation occurs. Some individuals, particularly the elderly and those who have had prolonged bed rest, may have faintness or syncope upon rapidly changing from a recumbent to an erect position, again due to vasodilatation. This phenomenon also occurs in persons who have vasodilatation as a result of dorso-lumbar sympathectomy and in those receiving antihypertensive compounds (Dibenamine® or hexamethonium). In a similar manner, syncope occurs with severe infection (pneumonia), extensive tissue damage, and anaphylaxis. Conditions associated with a decrease in blood volume, such as Addison's disease, excess sweating, and acute hemorrhage, may lead to syncope.

Some of the disorders that produce syncope as a result of disturbed cardiac function are listed in Table 4. By means of reflex stimulation of the vagus, the heart may be influenced to stop

TABLE 4

DISORDERS PRODUCING SYNCOPE AS A RESULT OF DISTURBED CARDIAC FUNCTION

1. Bradycardia
2. Asystole (Stokes-Adams)
3. Vagovagal
4. Pleurovagal
5. Peritoneovagal
6. Oculovagal

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7. Carotid sinus — cardiac type
8. Psychogenic vagotonia
9. Myocardial insufficiency
10. Coronary insufficiency
11. Ventricular fibrillation
12. Paroxysmal tachycardia
13. Aortic stenosis
14. Valsalva phenomenon

beating and, of course, when there is asystole for more than a very few seconds, syncope results. The afferent impulses leading to the vagus stimulation may arise in the pleura, peritoneum, eye, stomach, carotid sinus, brain, and many other sites. When there is disease of the cardiac conduction system, changes in rhythm may occur and in the process of changing there may be transient asystole — such is the situation with Stokes-Adams syndrome. When the myocardial contractions are weak, as may occur with myocardial ischemia or with ventricular fibrillation, syncope results. It also occurs with impediment to the ejection of blood from the heart, as with aortic stenosis. It is also associated with severe tachycardia, such as paroxysmal auricular tachycardia. In this stance the heart is beating so rapidly that it does not have opportunity to fill adequately.

Snycope occurs with a variety of conditions associated with impaired cerebral blood flow, such as: angiospasm, embolism, migraine, arteriosclerosis and other diseases of cerebral blood vessels.

Syncope also occurs with a great variety of conditions that are associated with abnormality in the composition of the blood. Examples of these are: 1) hypoglycemia, 2) hyperventilation, 3) anoxemia, 4) anemia, 5) tetanyhypocalcemia, and 6) reduction in blood volume.

Various diseases of the brain may produce syncope. Some of these conditions are: 1) epilepsy, 2) hysteria, 3) carotid-sinus syndrome, cerebral type, and 4) brain tumor, etc.

Although epilepsy may cause syncope, it is important to identify it since there are a number of important differences between the common type of syncope and classic epilepsy.

TABLE 5

DIFFERENCES IN COMMON TYPE SYNCOPE AND CLASSIC EPILEPSY

	EPILEPSY	*SYNCOPE*
Posture at onset	Any	Vertical
Incontinence	+	0
Tongue biting	+	0
Skin color	Flushed	Pale
Skin moisture	Hot and wet	Cold and wet
Breathing	Apnea; stertor	- - -
Duration	Long	Short
Confusion afterwards	+	0
Headache afterwards	+	0
Myalgia afterwards	+	0
EEG afterwards	60%	10%

Just as there are many causes of syncope, there are many different types of therapy. A few examples are 1) the recumbent or head lowered position of the patient, 2) administration of norepinephrine, 3) administration of atropine, 4) administration of quinidine and/or digitalis, and 5) administration of glucose, calcium, etc.

DIZZINESS

The information regarding vertigo and syncope is much more clearly defined than is the situation with dizziness. Dizziness is, indeed, a common complaint. Most of the conditions that cause syncope or vertigo may, in milder form, cause dizziness. Some disorders that not uncommonly are associated with dizziness are: 1) mental disturbances (psychoneurosis, schizophrenia), 2) brain tumors, aneurysms, etc., 3) cerebral arteriosclerosis, CNS syphilis, hypertension, 4) vasodepressor syndromes, 5) anemia, 6) anoxemia, and 7) "toxic disorders" ("biliousness", fever, infections).

CONCLUSION

Now, the question that you medical directors are interested in is, what are the insurance risks with individuals who have syncope, vertigo or dizziness? These symptoms may be manifestations of very serious disorders or they may be relatively trivial. Syncope and vertigo tend to be more serious than dizziness and usually are more definitive. Dizziness, like "gas on the stomach," may be

related to nervousness or to as serious a disorder as cancer. In order to determine which exists, one may have to perform very extensive examinations and then you may have to base your conclusion on probabilities. Where difficulties in the decision are eminent, it may be worthwhile to note changes over a period of several months. In the final analysis you probably would not reject a person because of dizziness alone, but it would make you be cautious about his acceptance.

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PRESIDENT LEE — You have given us a most instructive and clear-cut approach to this problem. I am sure, Dr. Williams, that what you have given us will become a textbook for reference in our underwriting manuals. There certainly must be some questions from our members.

UNIDENTIFIED SPEAKER — One of the chief things we are asked to underwrite in this group is the clinical history of Meniere's disease. In many cases, the person is a good risk except for this history. This presents great difficulty, and I have not yet accepted anyone in which Meniere's is a factor. Could you say a word about the prognosis of Meniere's disease. We have an idea that it is not too serious.

DR. WILLIAMS — The main question, as I understand it, is the prognosis of Meniere's disease. In the first place, the prognosis is going to depend a lot on what one designates as Meniere's disease. I feel as though most of the real authorities on the subject find it

is important, in order to be sure about it, that they not only have vertigo but also tinnitus. In addition to that, there are many other features, as, for example, the paroxysmal nature of the attacks. Accepting the fact that you are dealing only with pure Meniere's, the prognosis is at best not good. A real cure certainly is quite infrequent. There are some individuals who have spontaneous remission even without treatment. There are many who get very good results from ammonium chloride, potassium chloride, and water restriction. But, the mere fact that there have been so many treatments proposed within itself attests to the fact that treatment has not been successful, and in severe cases we must go ahead and resort to surgical measures.

DR. HOWARD B. BROWN — These conditions come to us not as a thing present at examination but as a history perhaps within a few months, perhaps within a year or two years, which usually was incompletely studied and the diagnosis or cause not definitely established.

Let us assume that our examination was negative. Would you suggest practical procedures that we could request of our examiners to separate the more innocuous causes for these symptoms from the more important ones such as cerebral arteriosclerosis.

DR. WILLIAMS — Well, in the first place, that is in line with some of my opening comments on the term "dizziness". That term is very loosely used and it may be used at times when one really has in mind mental confusion and vertigo. So, the first thing would be to clarify that situation and also to determine whether there is any relationship to posture or to the status of the bowel habits. Just go right down the line to see if one can correlate the symptoms with anything in particular. Then, after a very careful and complete analysis by means of the usual history and physical examination, there being only one attack and everything else negative, I should think one could essentially ignore it. If it has really been a very distressing situation and one which you wish to pursue further, then you should examine the ears for such simple things as wax which can disturb equilibrium. In other words, I think that one cannot make a single generalized statement as to what to do. One has to go right down the line, bearing in mind things of the type that I have listed here.

DR. EDWIN G. DEWIS — Assuming that the history is of true Meniere's disease, what kills those individuals? What shortens their lives?

DR. WILLIAMS — I do not know of anything specifically that kills them. Meniere's, within itself, does not. Of course, some commit suicide and shorten their lives in that way. One may get a syncope attack. But in general Meniere's in its passive form does not critically shorten life.

DR. JOHN M. LIVINGSTON — We frequently see reports of an acute short attack of labyrinthitis. It is thought to be of no consequence. You did not mention it in your talk and I wonder what your opinion is on that.

DR. WILLIAMS — That could be associated with a cold, disappearing quickly, without long-term significance. One of my colleagues had an episode a few weeks ago; within the last few days it cleared up and probably he will have no further difficulty. It is one of the commonest causes of the condition you described.

PRESIDENT LEE — Dr. Williams, I want to say again that I think you have given us a little textbook and that you have had a very appreciative audience here for your paper which they will want to peruse when it is published. And I want to thank you, Dr. Bennett, for your introduction.

Gentlemen, it gives me unusual pleasure to introduce to you our next speaker, who is Director of the Institute of Pathology at Western Reserve University. Dr. Alan Moritz and I were practically youngsters together and are very old friends. It is a great pleasure for me to be able to introduce him to a meeting in which I have the responsibility for the program. I am happy to present him to you now. Dr. Moritz.

TRAUMA AND HEART DISEASE

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The degenerative and inflammatory vascular changes which constitute the disease ordinarily referred to as arteriosclerosis or atherosclerosis probably result from a systemic disorder in lipid metabolism. There is no evidence that either the metabolic disturbances or the vascular lesions that result from them may be predisposed to or caused by a mechanical injury to any part of the body, by excessive physical exertion, or by a pressor episode associated with injury, pain, excitement or exertion.

The investigations of Dublin and Marks, Gertler and others, indicate that there is a strong familial predisposition to the occurrence of degenerative vascular disease. Thus, Dublin and Marks reported that the mortality rate of 350 men who were insured during the early part of this century and whose family histories disclosed that two siblings, both parents, or one sibling and one parent, had died prematurely of cardiovascular disease, exceeded by approximately 40 per cent the expected mortality rate in the general population of persons of comparable age and sex. Gertler and his collaborators found that the incidence of premature arteriosclerotic heart disease was twice as high in the parents of a group of persons who had developed clinically recognizable coronary disease under the age of 40 as it was in the comparable segment of the general population.

Such a constitutional predisposition to arteriosclerotic heart disease is also reflected by the structural characteristics or somatotype of the individual. Sheldon and his collaborators have found that there are three basic types of human body build; endomorphy or round softness, mesomorphy or muscular ruggedness, and ectomorphy or linear slenderness. Usually one of these three basic types is dominant. Using Sheldon's criteria for somatotyping, Gertler and his colleagues have found that the incidence of prema-

ture (under the age of 40 years) coronary arteriosclerosis is highest in the group classified as endomorphic mesomorphs. Coronary disease occurs very rarely in persons who are predominantly endomorphic or predominantly ectomorphic.

Still another means of recognizing an innate predisposition to the development of coronary disease has been suggested by the work of Gofman and others. This concept is based on the fact that constitutional differences are probably disclosed by chemotype as well as by somatotype. Thus, in Gertler's group of young men with coronary disease it was found that 42 per cent had a serum cholesterol of 350 mg. per 100 cc. or over, whereas only 6 per cent of his control group showed such an elevation. Since arteriosclerosis is almost certainly a disease of recurring episodes of exacerbation and remission, it is possible that those with coronary disease who had a low serum cholesterol were examined during a period of remission, whereas the 6 per cent of the noncoronary group who had elevated cholesterols may represent persons who have not yet, but who will develop vascular lesions if their metabolic disorder persists. Gofman observed that 91 per cent of persons with coronary disease had an increase in the 10-20 flotation class of serum lipid molecules, whereas increases of similar magnitude were found in less than 50 per cent of the controls. This is by no means a complete consideration of the features of the chemotype which may predispose to the development of premature atherosclerosis but it serves to indicate the probability that such a chemotype does exist.

A consideration of what is likely to happen to persons with coronary disease once its presence is established is also relevant to a discussion of trauma and heart disease. Bloch and colleagues have recently published a report of their follow-up studies of 6,000 people upon whom the clinical diagnosis of coronary disease had been established. Their findings indicate that the likelihood of death of a person known to have coronary disease is approximately three times as great as that of a comparable person in the general population during the first 5 years after the disease has been recognized. If the first 5 years is survived, the risk during the next 5 years is only about twice as great as that of the general population. If the first 10 years is survived, the man with a coronary history

is only 1.6 times as likely to die as the average man of his age in the general population. In evaluating these figures it should be borne in mind that the actual prognosis in coronary disease is probably not quite so good as these figures indicate, since they were derived from persons who survived their initial attack of coronary insufficiency long enough to go to the Mayo Clinic for examination. It is a fact that many persons die immediately or within a few weeks of the time that their first attack of coronary insufficiency was recognized. It is also a fact that many persons who at some time in their lives suffer from sufficiently severe coronary atherosclerosis to be recognized clinically, live out their normal expectancy. The longer the first attack is survived the better are the patient's chances to achieve average life expectancy.

In what circumstances may trauma or stress be capable of accelerating the development of coronary disease or of causing a harmful change in already existing vascular lesion?

It should be recognized that direct trauma to an already diseased vessel may be capable of damaging it in such a way that its lumen caliber is suddenly and significantly reduced. Thus it is a fact that a violent blow over the precordium which causes fracture of the sternum or of the ribs overlying the heart may cause bruising or laceration of a diseased segment of the descending ramus of the left coronary artery. The immediate consequence of such an injury may be the development of an intramural hematoma with resulting narrowing of the lumen and coronary insufficiency. If such an injury is sustained it should be immediately apparent.

Atherosclerotic plaques are frequently richly vascularized by large, thin-walled capillaries. It is conceivable that a direct trauma to the heart, or that a pressor episode caused by the exertion, excitement or pain incident to a trauma elsewhere in the body, may cause such thin-walled vessels to rupture, thereby leading to the formation of a subintimal hematoma with sudden reduction in lumen caliber of the vessel and circulatory insufficiency. If an injury to any part of the body is followed by secondary shock or if it necessitates bed rest and immobility, the likelihood of spontaneous thrombosis of a diseased coronary artery is enhanced. The only circumstance in which an injury may be held responsible for

coronary thrombosis by this mechanism is when the injury does result in shock and when the thrombosis develops during the period of circulatory failure.

A normal or even an elevated blood pressure may be required to force enough blood through a diseased and stenotic segment of a coronary artery in order to maintain cardiac function. It is apparent then that a hypotensive episode such as that which occurs during secondary shock may precipitate acute coronary insufficiency in a person not previously incapacitated if the degree of vascular narrowing present is such as to require a normal or elevated pressure to maintain an adequate flow of blood through the diseased vessels.

Still another possibility by which a trauma to any part of the body might conceivably cause a harmful change in an already established coronary lesion is by increasing the coagulability of the blood. It has frequently been asserted, although without general agreement, that mechanical disruption of the tissues anywhere in the body may lead to a temporary increase in the coagulability of the blood. In such circumstances it would be reasonable to believe that thrombosis would be more likely to occur at a site of existing vascular disease than elsewhere. If the coagulability of the blood were increased as a result of the traumatic injury, thrombosis of a diseased segment of a coronary artery might be caused to occur.

There is no reasonable doubt but that the imposition of an excessive work load on an already diseased heart may cause it to fail. Thus, if coronary disease is already established, the sudden increase in work load as a result of exertion or as a result of a pressor episode incident to an injury, may cause a previously competent heart to fail. However, if the failure of a diseased heart is to be attributed to any given injury or pressor episode, it should follow immediately after such an event. There should be no latent interval between the precipitating event and the development of heart failure if a causal relationship between the two is to be regarded as plausible.

The last and most important relationship to be considered is that of fortuitous coincidence. A large proportion of the population becomes disabled and dies because of arteriosclerotic heart disease. It is inevitable that the disability or death of many of these persons will be preceded by some remembered incident of

injury or stress. The ability of most persons to remember such events is tremendously enhanced by the prospect of double indemnity or workmen's compensation benefits if a cause and effect relationship between trauma and heart disease can be established. The overwhelming majority of such claims for compensation that have been brought to my attention represent nothing more than a fortuitous coincidence in which *post hoc ergo propter hoc* is cited as proof of eligibility for compensation.

PRESIDENT LEE — Dr. Moritz, you have certainly answered some questions very often asked in our business, and your paper will be a reference manual for us. We are most grateful and justly honored to have you here. There must be questions on this very vital subject.

DR. WILLIAMS — I think the Association owes a debt of gratitude to Dr. Lee for bringing us this last speaker. I had the privilege of knowing Dr. Moritz during a period when he was at Harvard where he certainly distinguished himself. I think his performance today is in keeping with that.

In regard to the term "somatic type", I think that is the term some people use instead of "genotype" because the latter is somewhat presumptuous. I do wish to say that a considerable proportion of the changes he presents are of the genetic type rather than hormonal. Yet the hormonal changes are quite important in the development of the arteriosclerotic process.

I did not hear Dr. Gofman yesterday. However, it has been clearly shown that the men have very much more coronary disease at an earlier period in life than the women, and it has been shown recently that estrogens can cause reversion of some of these chemical changes that are supposedly correlated with arteriosclerosis. There is evidence to indicate that if males are castrated early in life they develop less coronary disease.

There is one question I should like to ask Dr. Moritz, or any of you medical directors, because I have been very much interested in the subject. I have had the suspicion that one of the genetic deficiencies that might be associated with coronary disease is also associated with baldness. I have had the feeling that individuals who are baldheaded have a higher incidence of coronary arterio-

sclerosis, and I would be interested in knowing if anybody has any figures on that.

DR. MORITZ — I would like to refer that question to the medical directors!

PRESIDENT LEE — Thank you again, Dr. Moritz. As I previously stated, your discussion here will be long read in our Association.

The gentleman I want to introduce to you now is one whom you all know and who really needs no introduction. It is my very great pleasure to call to the platform Dr. David S. Garner, Chairman of the Medical Section of the American Life Convention.

DR. DAVID S. GARNER — Mr. President, Members and Guests of the Association of Life Insurance Medical Directors of America:

It is a distinct privilege as well as a very real pleasure to bring you greetings from the Medical Section of the American Life Convention. If I may, too, Mr. President, I wish to congratulate you on the excellence of your program and the meticulous care you have exercised in the arrangements for this meeting. Certainly no stone has been left unturned to make it one of the most informative and enjoyable in the long and enviable history of this Association. I should like to add also, and I believe that I voice the sentiments of everyone present when I say that we are very pleased that you and your Executive Council decided to hold this meeting in Los Angeles.

Plans have been made to hold the next meeting of the Medical Section of the American Life Convention at the Greenbriar Hotel at White Sulphur Springs, West Virginia, on Thursday, Friday, and Saturday, June 18, 19, and 20. The mornings, as you know, are devoted to scientific papers and discussions; the afternoons and evenings largely to recreation, such as golf, tennis, swimming, and bridge, or to the development of acquaintances and the renewing of friendships which have meant so much to each of us through the years.

Your Program Chairman, Dr. Norman Cole, is in the process of preparing a program which we hope will prove to be informative as well as useful in our work. It is not complete to date, and should any of you have any suggestions, I am certain that they

will be gladly received. It is our sincere hope that each of you and the many others who were not privileged to attend this meeting will be present and that you will bring the members of your family with you.

PRESIDENT LEE — Thank you, Dr. Garner.

The next speaker on our scientific schedule is Dr. Charles W. Barnett, Professor of Medicine, Stanford University School of Medicine. His subject is "Prognosis in Latent Syphilis." After talking this over with Dr. Barnett, I believe he has a fairly good idea of what our problems are. It is my impression that we are a bit antiquated in our handling of this particular disease in our underwriting work, due to, perhaps, failure to recognize modern concepts of therapy and what constitutes thorough treatment.

I am very happy, Dr. Barnett, that you could find time to take on this assignment, because you are, in my opinion, the best authority on the subject. I take great pleasure in introducing to you Dr. Barnett.

PROGNOSIS IN LATENT SYPHILIS

CHARLES W. BARNETT, M. D.
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Syphilis is a disease that has a much worse reputation than it deserves. It has a very bad name, but actually it is a fairly benign disease. In the last few years, since penicillin has come along, there is considerable opinion that syphilis may have been wiped out. I think this is dubious — at least we do not have any very good figures to indicate that. We do know that the character of syphilis has changed in that the early lesions of the disease are almost never seen any more. This is presumably due to the widespread use of penicillin, often without having had a diagnosis established; all of these lesions respond very quickly to penicillin. Whether or not the disease is actually being cured or simply being run underground, we will not know for a considerable time. However, syphilis has been prevalent enough and still is, and I think it will be a long time before it will be placed in the limbo of rare diseases. So far as insurance questions are concerned, it still deserves consideration.

Latent syphilis is that stage of the disease that is hidden. That is what the word "latent" means. There are no signs of the disease apparent. Therefore, it is a "disease" in which the patient is perfectly well. I am going to confine this discussion to latent syphilis, that is, cases where the disease has been present more than four years. The disease is transmissible only during the first four years. After that it is not transmissible, so at that point the Public Health authorities lose interest in it. You and I, and the customer himself primarily, are still interested in the latent stage.

About 20 years ago I became concerned with the question of the treatment of latent syphilis, because so often one would start with a perfectly healthy patient with a positive Wassermann, and would treat him for one or two years at considerable expense and a great deal of discomfort (and some actual hazard to life) and wind up with a perfectly healthy patient with a positive Wassermann.

It was extremely difficult to tell whether or not one had accomplished anything at all.

At the Stanford Clinic, we stopped treating some of these patients with latent syphilis. I do not think anybody else has done that. We did not stop treating all of them, but we have had some eight or nine hundred patients over a period of years to whom we have given no treatment whatever. When penicillin came in, we decided to review these cases and see whether or not we were right in letting them go without treatment.

There have been several studies made of latent syphilis in the mass — three in American literature. In all of these the assumption has been made that with chronic diseases of this kind one has to set up a minimum period of observation. These three surveys had a minimum period of two years in one case, five in another, and ten in another. None of these authors indicated why he picked these periods of observation. We presume it to have been simply because at that point the follow-up broke down.

We studied our figures in the conventional manner and tried several different periods of observation. I might say here that the evaluation of therapy in latent syphilis is difficult and has to be done backwards. You cannot evaluate it in terms of success, because most of the patients with latent syphilis live normal lives. If an untreated patient gets along perfectly well, and another you have treated also does well, you can hardly attribute the good results in the latter to the effect of treatment.

What we have to do is count the number of those who progress to the serious late stages; then by the incidence of progression, i.e., the incidence of treatment failure, we can compare one type of treatment with another or compare no treatment with treatment of some variety. When we lined up our data, using various minimum periods of observation, we found to our surprise and consternation that we could change the answers by the minimum period of observation we selected.

Table I illustrates this point. The "untreated" group represents the patients whom we decided to follow without giving any therapy. The "uncooperative" patients in the second column also received no treatment, or virtually none, but they made this decision them-

selves; that is, we elected to treat them, but they would not come in for treatment.

TABLE I

The Effect of Different Minimum Periods of Observation on the Apparent Incidence of Progression in Untreated Patients and in Patients Who Received Little Treatment Through Poor Cooperation.

Minimum Observation Period	*Incidence of Progression*	
	Untreated	Uncooperative
None (entire series)	2.5%	1.4%
1 year	3.9%	4.1%
3 years	4.8%	8.1%
5 years	5.3%	10.9%

If we take the entire survey, with no minimum period of observation, we find that 2.5 per cent of our "untreated" group showed clinical progression of the disease. Of the group not treated by their own choice, there were only 1.4 per cent progressions. From this it would seem that the "uncooperative" group were smarter than we were. However, if we compare the two groups after increasing periods of observation, after 5 years we are finally exonerated, and here our "untreated" group fares about twice as well as the "uncooperative" group.

There is obviously something wrong if you can arbitrarily select a minimum period of observation and completely reverse the incidence of progression from two to one in one direction to two to one in the other direction. The answer is in the cooperation of the patients. When you use a minimum period of observation, you will invariably find that the uncooperative group will have a higher rate of progression. The reason for this is quite obvious.

Looking at the "untreated" group in Table I again, these were patients who would come back reasonably well. When one did progress, we would find out relatively early. We would still have a considerable number of patients in the group so each progression would represent a fairly small increment in the percentage.

In the "uncooperative" group, when we tried to treat the patients they disappeared very promptly. The longer the period of observation, the fewer patients we had. A few would still progress. They

would get sick and have to come back. Each time one of these appeared, there was a tremendous jump in the incidence.

We started with, say, 1,000 individuals. In five years, the 5 per cent among the first group might represent 25 progressions. Over the 5 year period the total number left in the second group, the "unreliables," might drop down to 50. Ten per cent of this group would be only five progressions, and these five might have come back *because* of the progression — they had to. So this is a fallacious method of analyzing data. When one thinks about it, there does not seem to be much reason for having a minimum period of observation in this particular disease, because the time at which one of these individuals becomes known to us as a case of latent syphilis is largely a matter of chance. They are well as far as syphilis is concerned. The disease is picked up in routine examination, or because the individual has taken some psychological test, or for some other reason unrelated to syphilis. Some patients may appear relatively early in the period of latency, and some appear just as they are about to progress.

We should not set a particular period of observation, because the time we see the patient is meaningless as far as the disease is concerned. Consequently, it seemed to us, and I think this is correct, that instead of expressing progressions as a percentage of patients whom we have observed for a certain specified period of time, we should relate them to the total number of years of patient observation or total number of years of exposure to the risk of progression, beginning at the time when we first established the diagnosis and following the patient as long as we can. This method takes into account all the patients, or at least a more representative sample. Even more important, it does not weight those who have been followed for a longer period of time, and give them more value in the estimation of relapse.

Table II shows a comparison made in this way, the figures representing number of progressions per hundred patient-years of observation. The two columns indicate a division of patients into two groups according to the amount of previous treatment received before coming to our attention. Each of these groups was further subdivided according to the amount of treatment given them in our clinic ("late treatment").

TABLE II

PROGNOSIS IN LATE LATENT SYPHILIS
ALL TREATMENT VS. PROGRESSION

Late Treatment	Previous Treatment *Insignificant	Significant
None	2.1	0.4
**Little	1.2	0.8
Much	0.4	0.5

*Less than 10 doses
**Less than 55 doses of As and Bi

Comparison of the two columns shows that regardless of the amount of treatment we gave, there is a differential in favor of those who had a significant amount of previous treatment. Also, in the first column there is an orderly decrease in the incidence of progression with increasing amounts of "late treatment." This demonstrates quite clearly that anti-syphilis therapy does reduce the danger of progression in latent syphilis and is therefore worth while.

Penicillin has largely replaced arsenic and bismuth in the treatment of syphilis. It takes a long time to get data on the effectiveness of a new treatment for syphilis, and when we do find out something about penicillin, we will have to judge it by comparison with these older types of therapy that we have been using for many years.

TABLE III

PROGNOSIS IN LATE LATENT SYPHILIS
PENICILLIN VS. METAL CHEMOTHERAPY

Treatment	Cases	Prog.	Cent. observ.	Prog. per century
*As & Bi	1372	35	80	0.4
Pencillin	177	2	4	0.5

*More than 55 doses

Table III shows the data we have been able to gather up to now. After the study was completed, we tried to expand it by including the data from several other clinics in our area. Unfortunately, we were disappointed because the patients in the other clinics were

not studied carefully enough for inclusion with our data. The minimum requirement for the inclusion of a patient in such a study as this is that he must have had a careful physical examination before treatment to be sure he had latent syphilis, and a careful physical examination at the end of the treatment to be sure it had not progressed. However, Table III is included to point out that in the short period of time in this study we have had two progressions, so we know penicillin does not completely prevent progression.

These are 80 centuries of observation in the old series, and four centuries only in the new. Of course, with only two progressions one cannot actually draw any conclusions. It just happens that the magnitude of the incidence of progression is just about the same as we have had with the old type of treatment. We hope that with more figures that we will accumulate, we can show that penicillin is as effective as the older type of therapy.

We have had these two failures, and I think we know enough to feel fairly sure that one is not justified, as is all too frequently done, in simply giving a course of penicillin to anybody who has a doubtful serological test. "We won't take any chances. We will give you a course of penicillin. That will fix everything." We have no evidence whatever that it will fix everything. I think we have to be particularly careful to establish the diagnosis of latent syphilis before we treat it at all. We do not actually know that penicillin will cure it. We have some suspicious evidence that penicillin may not be as good as the older drugs.

TABLE IV

PROGNOSIS IN LATE LATENT SYPHILIS
TYPE OF THERAPY VS. SEROFASTNESS

Treatment	Cases	Serofast	Per cent
*As & Bi	1117	395	35%
Penicillin	254	123	48%

*More than 55 doses

Table IV shows the relationship of penicillin therapy to the old type of therapy with regard to Wassermann reversal. This happens to be from our own study.

One year after beginning treatment, the penicillin group had a

significantly higher proportion of positive Wassermann tests than those treated by the older methods.

These serological results may be worse than they look. The patients on arsenic and bismuth had all had a large amount of treatment, and most of them were still under treatment at the end of the year, whereas, the penicillin-treated ones had long since completed their treatment. We might expect some further reversals of Wassermann test results in the arsenic-bismuth group.

It has always been thought that serological results and clinical results did not parallel each other, and we have also believed that. From this study of ours, we have at least a suggestion that that may not be true, as is shown in Table V.

TABLE V

PROGNOSIS IN LATE LATENT SYPHILIS
SEROFASTNESS VS. PROGRESSION

	Cases	Prog.	Cent. observ.	Prog. per century
Fast	752	42	38	1.1
Not fast*	1718	50	92	0.54

*STS doubtful or negative after 1 year

The Wassermann-fast cases show 1.1 per cent progression per century of observation. In those whose Wassermann regressed, the incidence of progressions seems to be only about half. This does not actually prove anything, I am sure; but at least it carries with it the suggestion that possibly penicillin in latent syphilis will not be as good as the old type of therapy. However, I think for the moment we will have to assume that it is effective treatment.

Now the question arises as to how we can use these figures in estimating how much effect latent syphilis has upon the length of a person's life. There are three types of progression in latent syphilis. One is the gummata type. This is of no consequence as far as the life of the patient is concerned. Gummata are never fatal. They usually occur in the skin, sometimes in bone, and occasionally in the viscera. They respond beautifully to any kind of anti-syphilitic therapy. The incidence of fatality from them is negligible. I think we can eliminate this type of progression from consideration.

The most serious type of progression, as far as life is concerned, is cardiovascular. When the heart becomes involved, or the aorta is weakened to the point where it becomes dilated, then it is a hazard to life. It is very doubtful if the treatment can affect the disease after this has occurred. It may possibly slow the progression down a little but not very much. The primary concern, as far as life is concerned, is cardiovascular.

Neurosyphilis is also important. Here, again, if serious damage to the nervous system has been done, it cannot be reversed. However, penicillin has been extremely effective in controlling neurosyphilis — much more so than with cardiovascular involvement. The most serious type of neurosyphilis, as far as life is concerned, is paresis. It is controlled very nicely by penicillin and can usually be arrested unless the disease goes on a long time before the diagnosis is made.

In this study we have tried as much as possible to eliminate neurosyphilis from consideration. If the initial spinal fluid was positive, we did not include that individual in the study; so we have very little data on the incidence of neurosyphilis and its effect on life expectancy.

On the assumption that cardiovascular lesions are by far the most important from a life insurance standpoint, we went through our data and picked out the cardiovascular progressions. The results are shown in Table VI.

TABLE VI

THE INCIDENCE OF CARDIOVASCULAR PROGRESSION PER CENTURY OF PATIENT OBSERVATION IN RELATION TO TREATMENT

Subsequent Treatment	Previous Treatment	
	Insignificant*	Significant
Little**	0.62	0.18
Much	0.15	0.15

*Less than 10 doses

**Less than 55 doses of As & Bi

This represents a total of about 13,000 years of patient observation, or 130 centuries. Subdivisions were made according to the amount of previous treatment, and by amount of treatment in our

clinic. The patients who did not have very much treatment, either at our hands or before, had a progression incidence of .62 per century of exposure to risk. If we treated them, this dropped to about one fourth of that — .15 per cent. We can conclude from this table that we would have, for each 100 patient years, about .6 progressions for those relatively untreated, and .15 among those who had a reasonable amount of treatment either prior to the time we were able to see them or after we saw them.

I tried to convert this into the amount that would be subtracted from the life of the series of patients, that is, from the life expectancy of this entire group. This is probably an average group of people in which one might make the diagnosis of latent syphilis, and might be the type of people you would get during routine insurance examinations.

TABLE VII

AGE DISTRIBUTION AND NORMAL LIFE EXPECTANCY IN 2492 CASES OF LATENT SYPHILIS

Age	Cases	Expectancy in years	
		Individual	Total
20–	612	46	28,152
30–	841	37	31,117
40–	592	28	16,576
50–	284	20	5,600
60–	130	13	1,690
70–	33	7	231
		Total	83,446
			or 834 centuries

Table VII shows the average age distribution — about 2,500 individuals distributed according to decade. Column 3 shows the normal expectancy. On this basis, the total time we would expect these people to live would be 83,446 years.

Table VIII shows an attempt to tie these things together to see what effect cardiovascular syphilis would have. We have another series of patients whom we have identified with cardiovascular syphilis — 135 of them have died, and the average age at which these people died was 58.4 years. Taking that as a rough estimate

of the age at which these people die — treated or not treated — and taking the normal life expectancy of both men and women together, which is 67.7 years, it would appear that cardiovascular syphilis has cost each of these people 9.3 years of life.

TABLE VIII

PROGNOSIS IN LATE LATENT SYPHILIS

After life, 2,492 cases	834 centuries
Mean age of death, cardiovascular syphilis, 135 cases	58.4 years
Normal life	67.7 years
Loss per case of cardiovascular syphilis	9.3 years
UNTREATED: 1 cardiovascular prog. per 1.6 centuries, or 520 in 834 centuries. 520x.093 = 48 centuries lost. This is about 5.7% of the 834.	
TREATED: 1 cardiovascular prog. in 6.7 centuries or 125 in 834. 125x9.3 = 11.2 centuries lost. 11.2 is 1.4% of 834.	

Cardiovascular syphilis comes on late in life, and very seldom kills people early. There are several things we can do. Suppose we elect to disregard syphilis completely. Then the worst result we should get would be to take .6 progression per century of observation in patients who have not been treated much at all, either early or late. That is a worse result than one is likely to expect, for most patients who have latent syphilis have now had some treatment.

Assuming no treatment, we will expect one cardiovascular progression per 1.6 centuries or in 834 centuries the patients will have 520 progressions, each one costing the patient 9.3 years of life, amounting in all to 48 centuries — 5 per cent of the total. In treated patients, we would expect only 0.15 progressions per century observation, or about one progression per 6.7 centuries. This would indicate about 125 progressions out of 834 centuries observation, or a decrease of length of life for the total group of about 1.4 per cent.

The hazard of neurosyphilis is considerably less. I think the total effect on the mortality would be, perhaps, not over something like 2 per cent in the total life period of the entire group.

There are various things one might do, then, about insuring people who have latent syphilis. First, you might disregard it completely. The second would be to do a serological examination on everybody who applies for insurance; to do spinal fluid examinations on all positives and require that they all be treated.

A third might be, among the patients known to have the infection, from the history perhaps, to accept only those who have been treated.

The diagnosis of latent syphilis is becoming more difficult. With the new Treponema pallidum immobilization test, it is becoming evident that a lot of positive reactions, and particularly weakly positive ones, are false and do not indicate syphilis at all. If one undertakes a serological diagnosis of syphilis, it involves considerable testing and a certain period of observation. It might even involve the performance of this T. pallidum immobilization test which can be done now in only a very few places and in quite limited groups. If one undertakes the serological diagnosis of syphilis, it is a considerable chore, and I think if one did undertake that it would necessarily include spinal fluid examinations.

From these figures that we have, the best thing to do about latent syphilis, as far as insurability is concerned, is to disregard it completely. I do not believe latent syphilis adds a serious hazard to a patient's life. I think if one happens to know that a patient does have syphilis, it would be well to require that he have a course of penicillin before accepting him; not that we know penicillin will prevent trouble, but we are assuming that his chance of progression would be approximately one fourth of what it would otherwise be.

My feeling is that latent syphilis is a disease that has a much more evil reputation than it deserves — that its bark is worse than its bite. For insurance purposes, it probably could be completely disregarded.

PRESIDENT LEE — I think you will agree with me that this is a most revealing discussion and will offer much to help us in making certain changes in our underwriting. I am sure Dr. Barnett will be glad to respond to questions. Are there any questions?

DR. FRANK M. MCCHESNEY — I have seen several patients recently who have complained of hematuria. I have referred them to a urologist, and he found in some cases a papilloma on the bladder, and in some cases developing toward the malignant side. I know one or two of those patients had syphilis some time ago and possibly were inadequately treated. Some of the others may have had it also. My question is whether or not there are any data suggesting relationship between syphilis and malignancy of the bladder.

DR. BARNETT — I am quite sure there is not any relationship between syphilis and papilloma of the bladder or any other type of malignancy. There is an old saying that syphilis can simulate any disease. That is quite untrue. Syphilis follows pretty definite patterns, but many strange things have been blamed on syphilis. Once a patient has had syphilis, since we have no proof that we have ever cured anybody, it is a possibility to be considered when anything turns up as long as he lives. I am sure syphilis has been blamed for many things with which it has nothing to do. There is no evidence at all, that I know of, that there is any relationship between syphilis and any malignant growth.

DR. HARRY UNGERLEIDER — I want to call attention to a very significant observation made by Dr. Barnett when he said that syphilis gives a mortality rate of about 2 per cent. The observation I want to make is that there is a point of departure between life insurance medicine and clinical medicine. On the average of our policies, the premiums provide roughly for one death per thousand up to age 40. Two per cent would give 20 deaths per thousand. I do not believe we can disregard syphilis totally from the insurance standpoint. I am afraid, at the present state of our treatment we still have to consider it, because our premiums provide for very few deaths per thousand per year.

DR. BARNETT — As I said, I do not know to what extent an actuary would take figures of this kind into consideration. However, the figures of 1 to 2 per cent are not the number of people who die. That was the total shortening of the life period of the entire group. With all these latent syphilis patients together, most of whom as far as I know live perfectly normal lives, there would be out of 2,500 in that last treated group 125 only who would be

affected by this disease. Now, those 125 would have their lives shortened considerably. It would amount to 1 per cent of the total life of the whole group under the best circumstances, and 5 per cent of the total group under the worst circumstances — worse than I think one would ever get by disregarding the infection.

DR. NORMAN B. COLE — We hear rather loose phrases once in a while of "burned out" syphilis, meaning patients who become quite free of any symptoms without any treatment at all. I know Moore, of Baltimore, feels that a significant number of syphilitic patients just "burn out" after a while. I would like to know what you think about that and the proportion of such cases.

DR. BARNETT — I am sure, as I said before, that the majority of people who have untreated syphilis live perfectly normal lives. The actual number involved is not very well known because nobody has made any large survey of the people who have gone untreated, except for Beck many years ago in Sweden. On the basis of his report, we suspect that about two thirds of the people who get syphilis and are not treated at all will live perfectly normal lives and never get into any trouble of any kind. This "burnt out" thing is really the rule rather than the exception.

DR. EARLE T. DEWEY — If a man gets syphilis at the age of 20 and it is latent at the age of 30, is he any more of a risk than a man of 40 or 45? Are we safer to insure at 40 than at 30?

DR. BARNETT — I do not think I can answer that. If a man is old enough when he acquires the infection, say if he is 50, he probably cannot live long enough to acquire cardiovascular syphilis. This is one of the later manifestations of the disease. Ordinarily it becomes evident only after about 25 years. I presume the young man would be more likely to develop this type than the old man.

If you insure a man who has had his infection for 20 years, I think the chances of his getting cardiovascular syphilis are probably less than if you insure before that. Prior to 25 years he has an increasing chance, and after passing a peak, which is somewhere in that 20 to 25 year period, every year he lives his chances of getting it are presumably less. You cannot, I think, pin it down to figures.

PRESIDENT LEE — Doctor, there is a question that always arises when we know an applicant has latent syphilis or has had syphilis. What about the insurability of the wife in that regard, and what is the probability of risk in children from a father with latent syphilis?

DR. BARNETT — The insurability of the wife would depend entirely upon whether or not she had syphilis.

PRESIDENT LEE — I talked with you in San Francisco, and, if I remember correctly, you felt the incidence of transmission is not very great.

DR. BARNETT — I do not think you can say it is either universal or not great. If an untreated patient with syphilis is married within five years of infection, there is a pretty fair chance the wife will acquire it. If he acquires it after marriage, there is a chance the wife will get it. If he has had it five years, then the chances of the wife's getting it are negligible.

As for having syphilitic children, that does not occur except by the infection of the mother. As far as I know there are not any cases of syphilis transferred from father to children without infection of the mother.

PRESIDENT LEE — Thank you very much, Dr. Barnett. This has been a great contribution to our meeting. I am sure these gentlemen are all very grateful to you for helping clear this situation.

Our next subject is one that has aroused great interest in this organization. It seems to me that whenever I go East to one of our meetings, or the Medical Section meeting, at least half of the members say, "What about coccidioidomycosis? What about valley fever? Are they insurable for accident or sickness insurance? Are they insurable for life insurance?

We are fortunate to have with us today an authority on this subject, Dr. William A. Winn, Medical Director and Superintendent, Tulare-Kings Counties Joint Tuberculosis Hospital, Springville, California. I am sure that when Dr. Winn finishes his presentation all of your questions will have been answered. I want to say that Dr. Winn has certainly complimented us by graciously foregoing his annual deer shoot to be with us. I am pleased to introduce Dr. Winn.

COCCIDIOIDOMYCOSIS

WILLIAM A. WINN, M. D.
Medical Director and Superintendent
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Coccidioidomycosis is essentially a disease of the western part of the United States. Those of us who practice medicine in an endemic area, such as the southern end of the San Joaquin Valley, have learned to suspect coccidioidomycosis in almost every type of shadow that is demonstrable in an ordinary x-ray film of the chest. The etiology of the disease, its prevalence in certain geographic areas, its complications and residua, were really not understood until in 1937, when the so-called "renaissance" period in the study of the disease began with the discoveries of Gifford and Dickson, who first described the relationship between desert or valley fever and coccidioidal granuloma. Valley fever, also called California or San Joaquin fever, had been clinically recognized in the San Joaquin Valley by medical practitioners for many years, but it was not until these reports by Dickson and Gifford, some fifteen years ago, that this mysterious illness was recognized as a primary or initial phase of an infection produced by the fungus, *Coccidioides immitis*. And then, for the first time, the relationship between valley fever, and coccidioidal granuloma was understood, although the latter had been reported in Argentina in 1892, and in this country in 1894, following the observations of Rixford and Ophuls. The initial infection, better termed "primary coccidioidomycosis," instead of San Joaquin or valley fever, prevails in rather sharply limited geographic areas in the southwestern United States. These areas are characterized by hot, dry, dusty summers and rainfall almost entirely confined to a wet, winter season. Primary coccidioidomycosis is usually a benign, self-limited process that leads to recovery and the establishment of a permanent immunity. In three fourths of the cases, symptoms are so mild that the condition remains unrecognized, and its occurrence can only be proven by the development of skin sensitivity to coccidioidin. What is important is that the initial infection can on occasion be a phase preceding dissemination of the disease, resulting in widespread

involvement of body systems, and then a 50 per cent mortality. Primary coccidioidal infection may also leave chronic pulmonary changes, and pulmonary cavitation is just one of these residual changes that may bring a patient to the thoracic surgeon.

The causative agent is the fungus, *C. immitis,* which grows in the soil of the endemic areas, assuming then its vegetative or saprophytic phase. On solid culture medium it develops in the same way, producing a fluffy, cottony growth due to delicate branching hyphae, from which in turn are produced the chlamydospores. These spores, being very light, are wafted about by the valley and desert breezes, being carried with the dust. To the non-immune person they are highly infectious and as the western bound vacationer travels through certain areas of our southwestern states, he may inhale a bit of the spore-laden dust, and, ten to fourteen days later, develop primary coccidioidomycosis, even though by that time he may have returned to his native hearth and fireside in dear old New England. Or, the careless laboratory technician, uncovering the Petri dish to closely inspect a fluffy growth on his Sabouraud's medium, fails to notice a small cloud of fine particles which rise up with the cover, which being composed of dried out chlamydospores, drift into his respiratory system, resulting in an initial coccidioidal infection. If a non-infected person moves into an endemic area, the odds are 9 to 1 that he will acquire infection by the fungus within ten years. If he has the misfortune to encounter a dust storm he can acquire infection in a matter of minutes. All of which brings out the important fact that the practicing physician in any part of the United States, should keep in mind that a history of residence within, or even just travel through one of the endemic areas can be the pertinent bit of information pointing the way to the correct medical interpretation of an unusual acute respiratory infection, or a chronic type of pulmonary change discovered in a routine chest x-ray.

After the chlamydospore once enters the body it undergoes the parasitic phase of its growth, forming sporangia, or the characteristic spherules, with doubly refractile walls, and containing endospores. As the spherule matures, it ruptures, liberating the endospores, each of which in turn develops into another spherule, setting up a cycle of growth within the host. The spherule, in con-

trast to the chlamydospore, is not conducive to the spread of infection from person to person, and by clinical analogy there is support for this fact in that the disease is not transmitted by the ordinary routes of infection seen in other types of respiratory infection.

The known endemic areas comprise the desert-like country which extends from western Texas, along the Mexican border, through southern New Mexico, central and southern Arizona, southern Utah, the tip of Nevada and into the highly endemic southern San Joaquin Valley. North of Fresno the disease becomes spotty, although it extends farther along the western side of this great inland valley, as far north as Tracy. Occasionally it spills over the coast range to the west, occurring in dry parts of Ventura and Santa Barbara Counties. Spotty areas of infection also exist in San Bernardino, Riverside, and San Diego Counties. Much of this information was derived from war experiences, and is described in detail by C. E. Smith and other observers of a Commission on Epidemiological Survey, who in 1941–42 worked under the direction of the Preventive Medicine Service of the Office of the Surgeon General.

In 75 per cent of cases, the initial infection is subclinical, that is, it is so mild that it is not recognized and only skin testing with coccidioidin will indicate that previous infection has occurred.

The remaining 25 per cent constitutes the clinical group. These present an illness of variable severity followed by recovery in the vast majority of cases. In members of the white race, the primary infection will ordinarily clear or become focalized, and in not more than a quarter of one per cent of cases will dissemination occur. Racial variation in response to the infection is proven, and people of the dark-skinned races, such as the Negro, Filipino, and Mexican, are definitely susceptible to endogenous progression of the disease process. In the Negro, for example, dissemination occurs at least ten times as frequently as in members of the white race.

The primary infection is often accompanied by erythema nodosum or erythema multiforme. This skin rash will develop in 20 per cent of clinical cases, and is five times as frequent in women. These skin changes coincide with the development of sensitivity phenomena, the rash appearing at the peak of allergy. An x-ray

of the chest may reveal the presence of pulmonary involvement manifested by a patch of pneumonitis occurring in one or more areas of the lungs. A dense infiltrate, often nodular in type, may appear. Secondary hilar or mediastinal adenopathy is not uncommon and tends to persist; sometimes this finding is ominous, heralding approaching dissemination. Pulmonary cavitation is not infrequent, usually occurring in areas of consolidation and closing spontaneously. A simple pleuritic effusion may complicate the initial infection. These primary coccidioidal pulmonary lesions can closely simulate tuberculosis or even metastatic malignancy. In the differential diagnosis one must also exclude such conditions as tuberculosis, viral pneumonia, bronchopneumonia, lung abscess and other mycotic diseases. These x-ray changes will usually appear within the first week of the onset of the infection.

Symptomatology will vary considerably, from mild malaise to severe prostration. With the onset of fever, chest pain usually appears, is often substernal in type, and tends to persist. A cough, only slightly productive, is usually present. Generalized muscular pains, including backache, are common. Arthralgia is frequent and may be accompanied by some periarticular swelling and stiffness of the joints, especially the knees. Fever usually subsides slowly by the end of the second week. Convalescence may be prolonged by persistent lassitude, fatigability and a slow return of strength, sometimes requiring several months before there is a return to normal well-being.

Confronted by such a picture in a person who has recently lived or traveled through an endemic area, the physician will first proceed with the coccidioidin skin test. Sensitivity to coccidioidin usually develops by the third or fourth week following infection. The test is similar to the Mantoux tuberculin procedure with interpretation of the skin reaction made after 36 to 48 hours. Coccidioidin, which is prepared from *Coccidioides* cultures by a method similar to tuberculin production, is used in 0.1 cc. amounts and in dilutions of varying strength, usually from 1:10,000 to 1:100 dilution. If the skin rash is present, one must be cautious and use a high dilution of coccidioidin which may even then aggravate the erythema. This test is quite specific and only in the low dilutions such as 1:10 has there been reported an occasional cross reaction, in particular to the histoplasmin sensitive patient. It is very im-

portant that syringes, needles and the pans used to boil these instruments for coccidioidin skin testing be reserved only for such testing, and never contaminated with other skin testing agents, such as tuberculin. When carried out properly this skin test is a most useful screen in the differential diagnosis of unexplained pulmonary infection. In patients with disseminated disease, anergy is common, and in approximately 70 per cent of such cases there is failure of the skin to react to even a 1:10 dilution of coccidioidin.

The next step in confirming a suspected diagnosis of primary coccidioidomycosis is to carry out certain serologic studies as developed by C. E. Smith. It is necessary to withdraw 20 cc. of venous blood, using sterile precautions, and then to separate the serum aseptically, and to preserve it with a few drops of 1:10 aqueous solution merthiolate. This is transferred to a sterile container that can be mailed promptly to Dr. Smith's laboratory at Berkeley, California. There, using coccidioidin as an antigen, the titer of the complement fixation is determined and the presence or absence of precipitins demonstrated. With the presence of these humoral antibodies, the diagnosis becomes quite conclusive, and in our experience the test is both accurate and specific. I cannot recall ever having received a false positive report. These serologic studies are also of prognostic value, and Dr. Smith is often able to predict the severity and probable course of the infection by the degree of titer of the complement fixation. In return for this invaluable aid by this laboratory, the physician should submit a complete clinical abstract of the case, with specific information concerning history and date of exposure in an endemic area, giving also the date of onset of symptoms and their description, the x-ray and laboratory findings, including the blood sedimentation rate and results of coccidioidin and tuberculin skin tests.

It is not necessary to go to the trouble of isolating the infectious agent if the above steps have been carried out. This can be a complicated procedure and requires expert bacteriologic assistance. It is also hazardous inasmuch as the spores from mycelia are highly infectious to non-immune laboratory personnel. Bacteriologic evidence is necessary only when serology happens to be negative for specific antibodies and when, as in the instance of residual pulmonary cavitation, it becomes necessary to rule out tuberculosis.

Under these conditions, collections of sputum or tracheal wash material should be obtained and referred to a capable bacteriologist.

Other clinical studies of the patient should include a blood sedimentation rate determination by any accepted method, to indicate the degree of activity of the infection. The blood count may show a mild or moderately severe leucocytosis with occasionally a prominent eosinophilia.

Primary coccidioidal disease within the endemic areas is widespread and as it extends throughout the dry, warm summer months, a peak of infection of resident population results that is proportional to just how much cultivation of soil takes place, and therefore, to how much dust is created, and to how many susceptible non-infected persons inhale the spore-laden dust. The lower San Joaquin Valley is being intensively cultivated and through it travel many people along No. 99 highway, and so they also contribute, to a lesser extent, to the index of infection. Despite the fact that primary coccidioidal infection is common and widespread in the endemic areas and that much illness is thereby created, it still remains a disease from which recovery is the rule. Not more than 0.1 to 0.2 per cent of cases will progress to dissemination, and perhaps a similar very small percentage will be left with complicating pulmonary changes.

The insurability of a person who has completely recovered from the infection, and who has not inherited a residual pulmonary cavity, a coccidioma or localized bronchiectasis, is just as good as that of anyone. As a permanent resident of an endemic area, he is even a better risk than the susceptible individual who has just moved into the same geographic location. The non-immunized, uninfected, dark-skinned person, such as the Negro or Filipino farm worker, will have a more hazardous hurdle to take when he acquires his primary infection, because dissemination occurs in this race at least ten times as often as in the white-skinned race.

Dissemination (coccidioidal granuloma) is always serious and occurs when, due to failure of focalization of the primary infection, the spherules are carried through the vascular or lymphatic channels into other body tissues. The prognosis then becomes guarded and mortality rises to 50–60 per cent. Almost any of the body systems can become involved, with the possible exception of the intestinal

tract. Lymphadenitis, empyema, pericarditis, osteitis, meningitis, and skin infections are the rule, with abscess and sinus formation a typical part of the picture. C. E. Smith has shown that in white men not more than 1 in 100 of the clinically recognized instances of primary disease will disseminate. It is even a slightly less frequent occurrence in white women. If an analogy to tuberculosis is taken, the spread of the infection in dissemination is that of endogenous re-infection. There occurs an overwhelming invasion of rapidly self-multiplying organisms which comes about as a result of the spherule-endospore cycle of reproduction. In acute fulminating cases, the process takes place and exodus occurs within one to six months and mortality approaches 100 per cent. Chronic dissemination is a slower but still a continuous process dating from the initial infection, usually of 1 to 3 years duration, and bearing a somewhat lower mortality of 50–60 per cent.

Any history of dissemination can only be regarded, from the insurance standpoint, as ominous, unless there has been at least a five year period free of any form of recrudescence of disease and accompanied by favorable serologic findings and the absence of any sequelae or residual lesions.

When treating primary coccidioidal disease, the clinician must therefore remain constantly alert to the danger of dissemination and insist on adequate bed rest until focalization of the initial process has been accomplished. A prolongation of fever, or failure of any acute pulmonary lesion to clear, or the appearance of hilar adenopathy, a rising titer of complement fixation, a rapid blood sedimentation rate, any of these should make the physician wary of dissemination. And if his patient happens to be dark-skinned, he must be even more cautious and insist on prolonged bed rest.

No specific treatment has been found that is effective against *Coccidioides immitis* in the body. J. A. Schwartz has tested, in vitro, stilbamidine, actidione, Rimifon® and ethyl vanilate. In his hands none of these agents retarded the growth of the fungus on culture medium. Rimifon® has been tried in a dosage of 5–9 mg. per Kg. per day, but clinically has had no definite effect upon the disseminated disease. We have found slightly favorable results by using promizole, in doses of 12–20 Gm. daily, given by mouth

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for several months. In vitro, however, this drug has not been very promising. S. A. Waksman, at Rutgers University, has isolated an antibiotic in the form of a fungicidin which appears to have some definite effect against *C. immitis* but according to his last report the substance is still too toxic for human use. Lack's preparation of prodigiosin has been tried but no definite beneficial clinical results were shown. In addition to these recent attempts to control the disease, almost every variety of substance and chemical compound has been tried, including antibiotics and sulfonamide preparations, without success. Dr. Jacobsen's results with vaccine have been reported as successful in his hands but I do not know of any clinical corroboration.

When there is x-ray evidence of pulmonary involvement accompanying primary coccidioidal disease, it is usually manifested by an area of pneumonitis. Ordinarily, this clears within a month, only occasionally persisting for a longer period. Sometimes nodular densities form and these can be very slow in clearing and also closely simulate metastatic malignancy, unless they have been observed from the onset and are thereby correctly identified.

One of the important residua of primary coccidioidal infection is the solid solitary focus or coccidioma. This may be discovered following a chance x-ray of the chest and, because it can so closely simulate malignancy, it usually becomes necessary to carry out thoracotomy and perform a frozen-section tissue diagnosis to rule out a malignant lesion. These solid round foci can then be removed by simple segmental resection. This is probably advisable because they can undergo abscess formation, break down and form secondary cavities.

Calcification and fibrosis, residual to primary coccidioidal pneumonitis, are of no great clinical significance. Bronchiectatic change is infrequent and in those we have seen did not require surgical treatment.

Of the group of pulmonary residual lesions, pulmonary cavitation is the most frequently encountered and also the most intriguing. Such cavities must be separated from the primary type of cavity that occurs with the initial coccidioidal pulmonary infiltrate, and is a will-o'-the-wisp affair that comes and goes spon-

taneously. In contrast, the residual cavity may appear after the primary pneumonitis has cleared completely, and this type of cavitation tends to persist over a long period.

Some of our patients have been observed for as long as twelve years, during which time there has been little change in the x-ray appearance of the cavity. It is possible that some of these cavities develop from a small area of necrosis which produces an interruption of the normally unyielding elastic framework of the lung parenchyma. Then, because of the interplay of several factors, including elastic retraction of surrounding resilient lung, combined with a peripheral or marginal atelectasis of the bordering alveolar tissue, plus the ballooning effect of partial bronchial obstruction, there arises a mechanically developed cavity. This type of cavity formation is peculiar to coccidioidal disease and is conceivably not the direct result of an actively destructive infectious process. This theory is borne out by their x-ray and gross appearance, especially when they possess a thin-walled, cyst-like structure and there is no evidence of surrounding disease. They must be considered as rather benign stabilized defects which are the end results of a burned-out area of previous primary coccidioidal infection.

They are important for the following reasons: 1) They are often mistaken for tuberculous cavities, 2) 65 per cent of them produce hemoptysis, 3) 2 per cent of them rupture through the lung periphery producing spontaneous pneumothorax and coccidioidal empyema. Ordinarily, they tend to produce few symptoms or are only occasionally mildly suppurative. At Springville, we have followed a series of over 125 patients with such residual pulmonary cavitation and have reached the following impressions:

1. Those measuring less than 2 cm. in diameter, about 25 per cent of the group, do not require any specific treatment and will usually close spontaneously.

2. Those that are not too peripheral in location and therefore will not tend to rupture, and which do not measure over 4 cm. in diameter, can often be closed by simple collapse measures such as pneumothorax or pneumoperitoneum, sometimes supplemented by phrenic nerve paralysis of the corresponding diaphragm.

3. Those cavities over 4 cm. in diameter, or those that are peripheral in location, are best treated by surgical removal. This

usually means segmental resection or, if the cavity is firm enough, a simple shelling-out from the surrounding pulmonary tissue. Larger cavities measuring up to 12 cm. in diameter have been found and they require lobectomy and occasionally even pneumonectomy for successful extirpation. In 33 instances we have used such major surgical procedures at Springville to eradicate residual coccidioidal cavities. These patients have all made uneventful recoveries except for one instance of coccidioidal empyema which required a secondary thoracoplasty.

Cavities which are the cause of persistent bleeding will, regardless of how small they are, require either closure by collapse therapy or surgical removal.

One does not have to fear spread of the disease from these cavities, such as that which threatens from tuberculous cavities. From that standpoint alone, surgical eradication is not indicated when considering the coccidioidal cavity. Once the primary infection has healed or focalized, a sufficient degree of immunity is attained that effectively blocks off any endogenous re-infection by the fungus. This is a rather striking phenomenon that has been borne out by our long observation of many patients with such cavities who have followed a normal living routine over a period of years, with little change apparent in their chest x-rays. When these cavities are examined grossly, following surgical removal, they are usually found to contain the spherules of *C. immitis*, proving that there is a happy balance in the immunity-resistance mechanism between the body and the fungus, with the infective agent remaining confined to the cavity, and without provoking any surrounding reaction or extension of disease into adjacent lung tissue or other body systems.

In closing, I do hope that this scientific presentation will not ever keep any of you from visiting the San Joaquin Valley or perhaps enjoying some of its attractions, such as Sequoia National Park or the Kings River Canyon. After all, there are thousands of very healthy people living there in many thriving communities. If it will be of any reassurance or comfort to you, I myself, after 17 years of exposure therein, remain a horrible exception to everything that I have told you in that I am still skin-negative to Dr. Smith's most potent dilution of coccidioidin. The secret is to avoid

the wrong dust storm at the right time — and that's all you have to do.

PRESIDENT LEE — I am sure, gentlemen, you all enjoyed, as I did, the very thorough and interesting discussion as applied to our problem with this disease. Are there any questions on this subject that you would like to ask Dr. Winn?

DR. JAMES P. DONELAN — The boys who were stationed in the desert training areas after a period of several months would drift in to us and they would have these thin walled cavities. They would carry the cavities for years. You say that you have people residing in the Valley who have carried their cavities for four or five years. Are these people not the exception? If they have a small cavity should they not be accepted for life insurance?

DR. WINN — Remember these cavities are residual. Cavitation is not a prominent feature in this type of disease. Because of this, residual cavities are only a defect following the primary cavities. Insurability does not decrease as it does whenever there is a suggestion of a history of dissemination of disease.

PRESIDENT LEE — Am I correct in my impression that these patients, when we see them after recovery from a primary lesion which you indicated showed a very high percentage of recovery, are no more of a risk than anyone else as to recurrence and complications?

DR. WINN — That is correct. It is nothing more than a long drawn out pneumonia. If one is going to live in the endemic area, he is a better risk than the person who has not had it.

PRESIDENT LEE — The chronicity of the symptoms associated with the primary lesion is not usually too significant from the standpoint of insurance coverage.

DR. WINN — Twenty-five per cent of the clinical group — those are the people who have fairly severe symptoms — from the standpoint of sickness insurance may require up to six months of care because they will be unable to return to activity. But, remember that 75 per cent of the infections are subclinical. They are so mild that the infection is not recognized. They will treat themselves for a minor cold, a respiratory infection, and get over it.

PRESIDENT LEE — Thank you again, Dr. Winn. That answers many of our questions. You have made a great contribution to our specialty.

Our next speaker will discuss a subject that confuses, I think, many of us. That subject is "The Muscular Atrophies." I see these cases and consult the textbooks without finding a clear classification of these diseases. We are very fortunate to have with us an eminent local neurologist, Dr. John B. Doyle, who is another one of my friends whom I have imposed upon during this meeting. I want you to know he is your friend, too. He has done some wonderful work for my own and other companies on disability claims and on pre-analysis of risks with neurological problems. It is with great pleasure that I introduce to you my colleague, Dr. Doyle.

THE MUSCULAR ATROPHIES

JOHN B. DOYLE, M. D.
Los Angeles, California

When Virchow published Cellular Pathology in 1858, he established what Lord Lister described as the "true and fertile doctrine that every morbid structure consists of cells which have been derived from pre-existing cells as a progeny." At the time, brilliant clinicians who were describing new entities and syndromes were more than ever before stimulated by this doctrine to carry their investigations beyond the life of their patients to the laboratories of pathology. As case reports accumulated, it became possible to integrate facts derived from the clinical and pathological spheres, to set up classifications, to establish broad principles of pathology and to indicate transitional relationships between certain groups of apparently separate clinical entities.

Nowhere were transitional relationships more clearly exemplified in the course of time than in the field of the neural muscular atrophies and the myopathies. Thus, it gradually became apparent that progressive muscular atrophy, progressive bulbar palsy, amyotrophic lateral sclerosis, and in certain instances, primary lateral sclerosis are but variants of the same fundamental degenerative process. All are characterized by degeneration of the neural motor mechanism with involvement of the upper and lower motor neuron systems. In progressive muscular atrophy and progressive bulbar palsy the predominant involvement is in the lower motor cell groups. In primary lateral sclerosis, which should probably not be considered a definite clinical entity, the involvement is predominantly in the corticospinal or pyramidal tracts and their cells of origin, and in amyotrophic lateral sclerosis degeneration of the upper and lower motor neuron systems is clinically evident. A patient may present evidence of spastic paraplegia early in the course of his illness, and after many years develop a typical picture of amyotrophic lateral sclerosis. A patient with chronic progressive muscular atrophy may later develop signs of bulbar palsy.

It is still advisable, however, to discuss progressive muscular atrophy and amyotrophic lateral sclerosis as separate entities des-

pite the fact that in both clinical entities pathologic examination reveals degeneration of the upper and lower motor neuron systems.

Progressive muscular atrophy of the Aran-Duchenne type begins, as a rule, in middle life. The onset is usually insidious, and progress is relatively slow. Men are more commonly affected than women. The exact cause is not known. At present it is commonly accepted that the condition is due to abiotrophy in which the cells of the anterior horns function normally until a certain age and then begin to degenerate. As a rule the patient becomes aware of weakness and awkwardness of the hands associated with atrophy of the intrinsic muscles. If paresthesias are present they are generally mild and often transient in nature. Pain is absent. The weakness generally spreads from the hands to the forearms, arms, and shoulders, although the deltoid muscles may be involved relatively early. Certain muscles may be spared and more distant ones may be affected. Gradually the atrophy becomes more pronounced. The musculature of the lower limbs, particularly the flexors of the foot and leg, may be affected. Ultimately the reaction of degeneration may appear. Less commonly the process begins in the lower limbs. Fasciculations are found everywhere in the affected muscles. As the process extends upward, the bulbar nuclei may be involved resulting in weakness and atrophy of the tongue and faucial musculature leading to dysphonia and dysphagia, and ultimately to death.

While weakness is usually the presenting complaint of the patient, the flattening of the thenar and hypothenar eminence, the deepening of the interosseous spaces, and the development of the claw hand are more striking clinically. In the course of years, the atrophy and paralysis may become extreme so that the contours of the head of the humerus and the acromion become visible. The tendinous reflexes are retained until atrophy is almost complete.

The atrophy is accompanied by fascicular twitchings which are fine, rapid, flickering, spontaneous movements of muscle bundles. They are present in muscles undergoing degeneration and disappear when the muscular substance has completely atrophied. In contradistinction to fibrillations which result from complete destruction of motor neurons, fasciculations are due to progressive degeneration.

If the process progresses slowly, the patient becomes adept at finding ways of using muscles which are still able to contract. While the clinical course may be very slow, complete arrest and cure apparently never occur. The examination of the cerebrospinal fluid gives normal values throughout.

Amyotrophic lateral sclerosis is a disease which involves men more frequently than women, appears in middle life, and like progressive muscular atrophy is of unknown etiology. It is probable that trauma is not a factor in the development of either progressive muscular atrophy or amyotrophic lateral sclerosis. While heredity appears to be of importance in the development of entities of similar nature appearing in infancy, such as amyotonia congenita or Werdnig-Hoffmann's disease, it does not seem to be a significant etiologic factor in adults.

The onset is insidious. As a rule weakness and awkwardness in the upper limbs are the earliest and commonest symptoms of amyotrophic lateral sclerosis. Later, weakness of the legs may become obvious and is likely to be of spastic nature. In still other patients, difficulty with speech and swallowing occur relatively early. With development of bulbar involvement, articulation becomes indistinct and the voice becomes hoarse, swallowing becomes difficult especially for liquids, and uncontrollable laughing and crying may be encountered.

The involvement of the upper extremities is generally symmetrical. At first the intrinsic muscles of the hand are involved, followed by atrophy of the musculature of the forearm, arm, and shoulder girdle. In certain instances, atrophy also occurs in the musculature of the lower limbs and trunk. As in progressive muscular atrophy, fascicular twitchings are seen in the affected muscles and are usually numerous. The tendinous reflexes of the limbs are generally exaggerated and may be associated with Babinski's sign bilaterally. The abdominal reflexes are decreased or absent. If pain is present it is usually cramp-like in nature and is due to spastic influences.

In summary, patients with amyotrophic lateral sclerosis show atrophy and weakness, fasciculations and evidences of pyramidal tract involvement such as exaggerated tendinous reflexes, clonus and pathologic reflexes. The gradual onset in middle age, or the

latter half of life, of muscular atrophy and weakness of the upper limbs, with fasciculations and pyramidal tract involvement, serves to establish the diagnosis clinically. While the predominant involvement may be in the upper limbs, the lower limbs may be severely affected, even to the point of muscular atrophy. At any stage bulbar palsy may complicate the clinical picture.

Progressive bulbar paralysis or progressive bulbar palsy begins as a rule later in life and affects the cells of the motor nuclei of the fifth, seventh, ninth, tenth, and twelfth cranial nerves. The first difficulty observed is the use of consonants. As the atrophy becomes more advanced, the patient has difficulty enunciating words. Coincidently difficulty with swallowing becomes more and more troublesome, particularly for liquids which tend to regurgitate through the nose. Later solids cannot be swallowed. If the muscles of mastication become involved there may be difficulty in chewing. Fasciculations in the affected muscles may be common and are often very annoying. The differential diagnosis between progressive bulbar palsy and pseudobulbar palsy or involvement of the upper motor neuron system associated with control of the bulbar musculature offers little difficulty. This condition results as a rule from a multiplicity of cerebrovascular accidents with hemiplegia involving first one and then the other side. Atrophy and fascicular twitchings are absent and unmotivated, and uncontrollable laughter and weeping are often present.

The pathologic process in all of these entities involves the anterior horn cells. The degree of involvement parallels the state of the disease at which the examination is made. In certain regions cells may be almost absent. In others an active progressive degenerative process may be present characterized by swelling of the cells with various stages of nuclear degeneration. Glial proliferation occurs after the degeneration of the cells and results in the formation of a diffuse glial isomorphic scar.

Paralleling the changes in the anterior horn cells the muscular fibers become edematous and lose longitudinal and cross striations. Later they split longitudinally and show sarcolemmal nuclear proliferation. The end result is replacement of the muscle by connective tissue.

The pathogenesis of the lateral or pyramidal tract involvement

is characterized by the progressive degeneration of the large Betz cells of the motor cortex, particularly in the region of the paracentral lobule, the origin of the fibers which innervate the lower limbs. The differential diagnosis involves amyotrophic meningomyelitis luetica, cervical pachymeningitis, cervical intervertebral disc syndromes, cervical spinal cord tumors, and syringomyelia.

Intermediate between the muscular atrophies and the myopathies is peroneal muscular atrophy or neural or neuritic muscular atrophy of Charcot-Marie-Tooth. This is a relatively common heredo-familial degenerative process involving the peripheral nerves and resulting in muscular atrophy of certain groups of muscles notably the peroneal muscles of the leg. This entity is generally traceable through several generations and may involve siblings or cousins. The sexes are equally involved and either sex may transmit it.

The earliest changes are noted in the muscles supplied by the branches of the peroneal nerves which become shrunken and degenerated. Later motor fibers of all of the nerve trunks supplying the distal parts of the extremities are affected. The process is generally much more pronounced in the lower limbs than in the upper limbs and may be associated in certain instances with the presence of fascicular twitchings. Only mild changes of degenerative nature are found in the motor cells of the gray matter of the spinal cord. In more advanced instances, slight degenerative changes are demonstrable in the pyramidal tracts and in the posterior columns.

As a rule, the age of onset is between five and fifteen years. The feet are inverted early due to peroneal weakness. When the anterior tibial muscles become involved, footdrop occurs with development of pes cavus and claw toes. Progress may be exceedingly insidious and may even become arrested. This condition does not interfere with life, though it may be partially disabling. Accordingly, orthopedic measures designed to stabilize joints are justifiable.

Progressive muscular dystrophy is a form of muscular wasting which has been described under many forms. It appears to be a primary disease of the muscles and is not associated with spinal disease or degenerative changes. Spiller has set forth clearly cer-

tain essential differences between progressive muscular atrophy and progressive muscular dystrophy. Progressive muscular dystrophy begins as a rule early in life and is frequently hereditary or familial; the prognosis as to life is much better in progressive muscular dystrophy; the trunk, pelvic, and shoulder girdle muscles are implicated before the distal portions of the extremities; fascicular twitchings are not encountered in this condition; and true reactions of degeneration never occur.

On the basis of specific localization of the muscles affected, progressive muscular dystrophy has been classified under many different heads. The clinical history generally begins in early childhood with disturbance of gait of waddling nature, followed by difficulty extending the lower portion of the trunk. To compensate for the weakness of the thigh muscles and the extensors of the trunk, the child usually develops a lordotic position with protruded abdomen. When the muscles of the shoulder girdle are involved the scapulae may be "winged out". The distal portions of the extremities tend to be free from involvement. The weakened muscles may be of normal size or even larger than normal. In other instances, atrophy becomes apparent relatively early in the clinical course. Microscopic examination shows that the muscular enlargement is due to pseudohypertrophy resulting from fatty degenerative changes.

In the facioscapulohumeral or Landouzy-Dejerine type of involvement the facial muscles are involved, resulting in the appearance of the myopathic smile and a mask-like expression of the face. At times the eyelids cannot be closed. The deep reflexes are diminished and may be lost; they are never exaggerated. True reaction of degeneration never appears. While the pseudohypertrophic type commonly has its onset in the first five years of life, the facioscapulohumeral type generally begins between twelve and fourteen years of age. Treatment is unavailing.

The essential pathology is in the muscle fibers which swell to large size as the striations break up and the sarcoplasm becomes homogeneous and glossy in appearance. Coincidentally, large vacuoles containing fat appear which gradually replace the bulk of the muscular tissue.

One of the transitional conditions of great interest is myotonia

dystrophica. In this condition there is progressive muscular atrophy without fasciculations involving particularly the sternocleidomastoid muscles, the quadriceps femoris and less frequently the muscles of the hands and forearms. The tendinous reflexes may be diminished or absent. Other conditions frequently associated with this state are cataract, testicular atrophy, and impotence. Coronary sclerosis is a frequent concomitant. As a rule the disease becomes apparent during the third or fourth decades. By some this condition is thought to be a late stage of myotonia congenita or Thomsen's disease.

Myotonia congenita usually affects several members of the same family, involves chiefly males, is present from infancy but frequently only becomes evident about puberty, and is characterized by increased tonicity of the musculature so that after a period of rest the muscle is moved with difficulty to contract. After one movement has been performed with great strength, such as grasping an object, the muscles are relaxed with difficulty. After several efforts, however, the movements may become free. All of the muscles of the body as a rule are more or less involved but the affection may be pronounced in certain parts. Emotional stimuli and cold aggravate the condition, while warmth diminishes it. The muscles frequently appear large but the patients are often quite weak. Microscopically the sarcoplasm is increased in amount and the sarcolemmal nuclei are multiplied. This condition is materially improved following the administration of quinine.

In summary, progressive neural atrophies are characterized by degeneration of the upper and lower motor neuron systems and comprise progressive muscular atrophy, progressive bulbar palsy, amyotrophic lateral sclerosis and primary lateral sclerosis. In the case of primary lateral sclerosis, the process is limited to the pyramidal tracts and their cells of origin in the motor cortex. The lower limbs are chiefly involved, resulting in spastic paraplegia. When this condition is encountered, it is well to remember that if the patient lives sufficiently long it is probable he will develop other symptoms. In one instance, a patient developed a typical picture of amyotrophic lateral sclerosis more than twenty-five years after a diagnosis of primary lateral sclerosis had been made. It was only during the last eighteen months of life that evidence of degeneration of the lower motor cells in the anterior horns of the gray

matter of the spinal cord, and later in the bulbar motor nuclei were discernible. In amyotrophic lateral sclerosis, atrophy of the musculature of the upper limbs and definite evidence of pyramidal tract involvement are present. Bulbar involvement may occur with or without evidence of upper motor neuron degeneration. In progressive muscular atrophy it is noteworthy that, despite considerable muscular atrophy, the tendinous reflexes as a rule are not materially diminished or lost. In this condition, however, the involvement of the lower motor neuron predominates to such an extent as to produce a clinical picture chiefly attributable to involvement of the anterior horn cells. Bulbar palsy is one manifestation of progressive muscular atrophy and is characterized by dominance of the clinical findings attributable to degeneration of the cells in the nuclei of the motor nerves distributed to the bulbar musculature. Pseudobulbar palsy, on the other hand, does not belong in this category. It represents the peculiar clinical picture that arises when the corticobulbar fibers are involved bilaterally and usually appears only after multiple cerebrovascular accidents resulting in hemiplegia on both sides.

In all of these conditions arising in adults there is little or no evidence to indicate heredofamilial predisposition. It is commonly agreed, however, that abiotrophy or premature degeneration of groups of cells is the most tenable assumption in the light of current knowledge. No satisfactory therapy has been evolved for any of these conditions.

Amyotonia congenita, or Oppenheim's disease, and infantile spinal amyotrophy, or Werdnig-Hoffmann's disease, are very rare conditions which probably represent, respectively, cases which run their course during fetal life, and cases which develop in early childhood and progress to fatality. From a pathologic viewpoint, both show involvement of upper and lower motor neurons.

Charcot-Marie-Tooth's disease represents an intermediate type of disorder between the atrophies and the dystrophies.

Progressive muscular dystrophy, on the other hand, represents an heredofamilial type of ailment affecting the muscles particularly of the shoulder and pelvic girdles, the neck and the facial region. The pseudohypertrophic type not infrequently begins

during the first five years of life, while the facioscapulohumeral type becomes apparent as a rule during adolescence or even later. Though it is generally progressive, it may be arrested in certain patients so that they may live thirty, forty, or more years after evidence of the disease is first noted. It is characterized by atrophy of the muscles in certain instances. In others the muscular bulk remains good or it may appear Herculean. The weak muscles of normal or large size are characterized histologically by fatty degeneration. True reactions of degeneration, however, are not encountered despite the fact that the responses to the galvanic and faradic types of current may be materially diminished. The reflexes in progressive muscular dystrophy are as a rule diminished or lost. No satisfactory form of therapy is available. On the other hand, muscular dystrophy may be complicated by myotonia. In this condition the involvement of muscles is chiefly in the region of the neck and face and the distal portions of the limbs, and is of atrophic nature. To some investigators myotonic dystrophy has seemed to be only a late stage of myotonia congenita, a familial and hereditary condition which is usually present from childhood and which is relieved by administration of quinine.

PRESIDENT LEE — Dr. Doyle, I think your presentation will be the medical directors' textbook hereafter for reference when these questions arise.

I want to ask now for any questions and I am sure Dr. Doyle will be glad to answer them.

DR. KENNETH F. BRANDON — I wonder if I might ask Dr. Doyle about the sign of fibrillary contractions in apparently healthy persons. We occasionally see people with these contractions in their calf or deltoid areas. There is no neuropathology or micropathology evident, and we have followed some of them for weeks and months and years and the contractions seem to continue. It is not a question of exposure to cold or fatigue. I wonder if you would comment on the significance and the cause, and of course our interest is in the prognosis.

DR. DOYLE — Dr. Brandon has touched on a subject that is receiving much attention right now and a subject for discussion among neurologists for many years. In 1951, Langley and Cato observed that if one severed the nerve to a striate muscle and

watched very closely the muscle which was exposed, within a few days the muscle would begin to show an infinite number of fine rapid twitchings. He called this condition fibrillation. The clinicians had already begun to use that term many years before. DeChine had described the fibrillary twitchings as what we now know as fibrillations in muscular atrophy.

It was not, however, until the late 1930's, after the development of the oscillographic technic, that much of anything was known about it. In 1938, there appeared an article in "Brain" in which they made some tremendous contributions to this subject. They showed that if a muscle is deprived totally of its innervation it will begin to fibrillate at the end of about five days, and these fibrillations will represent contractions of very rapid and very short nature, limited to isolated muscle fibers. This condition occurs only when the nerve fiber to that particular one that contracts has been destroyed.

Obviously, that was not the kind of thing that clinicians were talking about when they referred to what they saw as fibrillary twitching. A little further investigation showed that what we had called fibrillations were really contractions of groups of cells. Now a single motor neuron innervates approximately 150 muscle fibers, and it is contraction of a fraction or all of the motor fibers in a given bundle by a motor unit that results in the twitching that we see.

The only place we see true fibrillations is in structures which are particularly visible, such as the tongue where the thin mucous membrane makes it possible to see the very rapid movements. On rare occasions in very thin people, something of the same order may be seen in the deltoid, but the twitchings we have been talking about are not the twitchings of one fiber but of groups of fibers. It is one motor unit and all the fibers which it innervates, which might be 100 or 150.

When we have a chronic degenerative process going on in the anterior cells, with gradual loss of function, we have fascicular twitchings. We have fibrillary twitchings only when a given fiber has lost its innervation.

There is a third type of twitching, a so-called contraction, that has been observed repeatedly after old injuries and particularly

after polio of long standing. Not infrequently these patients will exhibit fascicular twitching, and these twitchings, if the patient is closely watched, will be observed to occur only when the patient begins a movement of muscular nature. They do not have the same significance as the fascicular twitching of group two which will probably continue to progress to fatality. In the third group there is simply an impairment in the function of a muscle.

The condition Dr. Brandon talked about is called myoischemia and occurs in perfectly well people who are particularly prone to sweat. What the relationship may be to sweating is not known. It certainly has very little to do with the salt or sodium chloride balance because the giving of sodium chloride and calcium does not benefit them. They occur in these individuals when they are fatigued and after prolonged stress. If one studies the fasciculations themselves, they are much slower and they are longer in duration. The patient is quite well in every respect. He has normal reflex reactions and no disturbances of any other nature.

PRESIDENT LEE — As I said to you before, Dr. Doyle, there has not been a very clear classification of these things from our standpoint, certainly not clear nor concise as to prognosis. Thank you very much for your valuable contribution.

There is a very important, everyday, across-the-desk, practical problem which confronts us, and I have asked Dr. John W. Wear to give us some of his observations as a Medical Referee with the Aetna Life Insurance Company. Dr. Wear.

OBSERVATIONS OF A MEDICAL REFEREE

JOHN W. WEAR, M. D.
Western Medical Referee
Aetna Life Insurance Company

In 1936, Dr. Cragin wrote to me about his purpose in placing a medical referee on the West Coast who would have charge of the appointment, discontinuance, and supervision of all examiners for the Aetna Life Insurance Company in the western territory, as well as being arbiter where there was a difference in medical opinion and, further, to adjust all complaints regarding medical service to the agencies.

Since I had been Medical Director in charge of all phases of underwriting for a small midwestern company for twelve years, the nature of the work outlined by him was quite familiar. He accompanied me west and formally introduced me to the agencies which would be under my supervision. There were 15 agencies from the Texas Panhandle and Colorado to the West Coast. When he departed for Hartford he said, "See that we have good examiners and that the agencies get the necessary service. You are on your own." This was encouraging and a challenge, for it showed he was neither mental nor muscle bound but welcomed any ideas that I might have. He always gave me full support, and was a grand person with whom to work. I have continued to receive the same support from Dr. Irving.

My first objective was to get acquainted with the territory, the men who were writing the business, and the doctors who were examining the cases. This entailed extensive traveling. I drove 162,000 miles the first 6 years, and in addition, used the train, bus, and airplane. I was not satisfied until every examiner was met wherever we had a resident agent. I also visited the examiners in the small towns adjacent to the cities where our general agents are located. During these visits, I reminded the doctor that all of us were primarily engaged in a great humanitarian work in helping to protect with adequate life insurance as many homes as possible. Where there is ample insurance, doctors and hospital bills are promptly paid as well as funeral costs, and

mortgages can be cancelled so that the widow and children can live as the father desired.

I also discussed our underwriting methods and problems, and went over the questions on our medical blank. Seventy-five per cent of the doctors showed an interest and remarked that it was the first time any one from the medical department of any company had ever called upon them. Twenty-five per cent appeared indifferent, or had serious physical impairments which unfitted them for our work, e.g. deafness, senility, slovenly kept office, or retrogression. These men were replaced.

I always invited suggestions for improving our relations, if none was volunteered. However, in most instances the examiner did not need an invitation but asked many pertinent questions. You will be interested in his questions and observations. The following were asked most often:

1. Why is the agent always in such a rush to get his applicant examined?

2. Why does he bring his applicant to my office during my busiest hours, and expect to get him examined right away?

3. I have noticed when I get a couple of rejections, the agents take their applicants elsewhere.

4. Why do agents make an appointment at a place of business where there is no privacy?

His questions were easily answered, and I feel sure he has a better understanding of the salesman's problems; but these questions were discussed with the general agent, also. For, obviously, the agents involved needed instruction. They had acquired faulty habits which the general agent should have corrected; but he could not correct them unless he knew about the complaints. It has been my practice to ask the examiner to report unfavorable experiences to the general agent, or to write to me. On many occasions the general agent has asked me to address the agents; this gave me an opportunity to talk about underwriting, getting the applicant examined, delivering policies issued in a special class, and how to get and keep the examiner's cooperation.

Life insurance is sold by informed aggressive salesmen who sincerely believe they are engaged in an essential business, which,

of course, is true. The examination is recognized as necessary but considered by both the salesman and the applicant as a nuisance in the consummation of a business transaction. Hence the doctor is accepted more on a business basis than professional. The sensitive physician will not be happy in our work. He needs a good sense of humor.

The examiner devotes the majority of his time to his patients and expects the same relationship with the applicant that exists with patients. He does not understand why there is a lack of cooperation in revealing a history, or resentment often shown when a physical impairment is found on examination.

One can often make progress by learning what to do when what he has always done no longer works. In getting a history, some applicants give a negative answer almost before the question is asked. We have suggested to the examiner that he complete the examination, fold the papers, place them in an envelope, and put it in a desk drawer out of sight. Then lean back in his chair and wait while the applicant is dressing, making some off-hand remark, e.g., "Strange that one of your age has never had an illness or consulted a doctor." You will be surprised how often he will reply, "Well, since the examination is over, I did see Dr. Jones for some stomach trouble" — then proceed to give a history which was not admitted previously.

The applicant and agent almost invariably ask the examiner whether he thinks he will pass. We have requested him to answer that he does not know what the company will do, for it has its own methods of classifying applicants for insurance, and there are reasons other than medical that lead to declination. This takes him out of the picture and he will not be bothered by either returning to inquire why he was declined or offered a policy in a special class.

There were other remarks by examiners directly involving the medical departments, e.g.,:

1. "The information which I give companies should be kept confidential. I have incurred the ill will of former patients because the information which I gave to the company was reported back to him by the agent."
2. "Why doesn't a medical director correspond with me about an examination instead of allowing clerks and lay people to do so?"

3. "The tone of the letter about differences in the history or physical examination is not always free from an inference of carelessness, which is not justified. I can record only the history which is revealed to me, and physical findings are not always static."
4. "I do not object to re-checking a history or any phase of the examination but it would be helpful, and the company would benefit by taking me more into their confidence. I do not like vague innuendoes."
5. "I like to feel that I am a representative of the company, but the manner of my appointment is not always conducive to this relationship. My only contact, direct or indirect, is the agent or some clerk."
6. "Why doesn't the medical department give us some of the statistical data which they use in classifying applicants? It would add to the interest of our work."

It is impossible for me to understand why the examiner's confidential information should be revealed. This is rightly resented by the doctor and has been the direct cause for many resignations and refusals to make examinations for life insurance companies.

The medical director does not have time to personally answer all the correspondence which comes to his department. There is no reason why a well trained layman cannot relieve him of routine matters. However, he should train his assistants so that letters are phrased so as not to arouse resentment. I do not feel there is any place for sarcasm in a business or professional correspondence. It only arouses antagonism. We know that pathologic changes are often kaleidoscopic. Give the examiner the benefit of this fact unless you are convinced he is either careless or incompetent. Then he should be discontinued.

I can see no reason why the examiner should not be told why a re-check is requested. This could be done without revealing the source of our information. If the examiner knows that in a previous examination an impairment was reported, he will not only be more interested in his re-check, but alert for any possible complications. I would like to see these Proceedings sent to every examiner. A method would have to be worked out to avoid duplications.

The question of fees is not now a complaint, since most companies now pay $7.50 for a regular life insurance examination. However, prior to the increase it was a serious problem. Many of our very best examiners were on the verge of quitting, and we were unable to get replacements with the qualifications that we wanted at the old fee.

My purpose in visiting an examiner, or in considering a doctor for an appointment, is to see his office equipment, to learn something of his personality, to see if he is interested in our work and whether he is too busy to give us the essential service, and to find out if he will make definite appointments, because an applicant will not sit in a crowded reception room waiting for his turn; and further, to go over our examination blank, answering any questions relating to it. These visits enable me to explain group statistical selection as well as to discuss the agent's difficulty many times of getting the applicant into the doctor's office.

Most companies receive letters from physicians requesting to be placed on their panels. These come, in most instances, from doctors who are relocating, or young men who are just getting started. Too often they lose interest after getting established. We prefer men who are already established, and who show an interest, but we encounter many instances of having to sell a high-class physician on the desirability of becoming an examiner. They relate unfavorable experiences with overzealous salesmen, or letters from home offices which were irritating. They complain of too much clerical work, and ask why the questions of minor significance cannot be deleted. There is a feeling among many physicians that the medical departments of companies are out of touch with the problems of private practice, the advances in clinical medicine, and that our statistical data does not take into consideration the spectacular advances in therapy.

If he received a copy of these Proceedings, it would show that we are informed. I have been successful in most instances in satisfactorily answering their objections and complaints. They usually seemed pleased to hear my explanations. We can get high class medical work and cooperation, but our efforts must be broadened to include the general agent or managers and the salesman. These experiences cause me to wonder if the medical departments of

many companies are not negligent in their public relations, or fail to pursue the reasons for requests to make changes or additions to their staff. One can always profit by asking and listening. Then ask and listen some more before acting.

It is not easy to build and keep a staff of well trained examiners who are interested and willing to give the service which we must have. We prefer internists with American Board qualifications when we can get them. In addition, we have young men who are getting established and who are willing to make evening home appointments. They are encouraged to do this as an excellent means of making new contacts. We have an understanding with them that if they expect to build and keep a satisfactory income from life insurance examinations, appointments must be kept. It is our policy to have as few examiners as possible in a locality. We have found that there is nothing to equal the receipt of a sizable check regularly to acquaint the examiner with our standard, and to the rendering of good service to the salesman. A doctor's interest cannot be maintained by an occasional examination.

When an examiner is needed, we visit the city and make inquiry among contacts that we have previously established, obtaining the names of two or three young doctors who are looking forward to careers as internists. We then make a social call upon each, selecting one with a pleasing personality who expresses an interest and agrees to give service. Then he is invited to have lunch with the general agent and myself. We have found these luncheons invaluable. Everyone is relaxed. The general agent feels free to tell the doctor about his problems of recruiting and training salesmen, and to explain the difficulties of the new agent, and further, to ask the doctor's forbearance if the new agent makes an unusual request for an appointment, or fails to keep one. We then enter the conversation and request the doctor to notify the general agent if this happens too frequently, or to write to me. We further suggest that the general agent have the new examiner present at the next agency meeting so he can meet the agents.

This program requires the assistance of the general agent, for, if he is satisfied he will take care of the agent's complaints and feel well enough acquainted with the newly appointed examiner to discuss any irritating grievances. Getting satisfactory appoint-

ments for examinations is a sales problem and a very important one from the general agent's and the salesman's viewpoint, as well as from the medical department and the company. The general agent will agree that in 90 per cent of instances, a well trained salesman can designate the time and place of the examination. It is usually the inexperienced or poorly trained salesman who has difficulty with his appointments. Many successful salesmen tell me fixing the time and place of the examination is not a problem. The salesman's attitude is largely a reflection of the general agent's or manager's. Often the general agent asks me to talk on the subject at a regular agency meeting, or discuss the question with an agent who is having difficulty.

Selling life insurance is not easy, as evidenced by the large turnover in the sales force of all companies. Consequently, we are as helpful as possible in freeing the agent's mind of any real or fanciful grievances, and in assisting him in getting medical service, and in freely discussing the necessity of sound underwriting practices. I have gone with the salesman many times to explain to the applicant the reason for the issuance of his policy in a special class. It gives me a real thrill when I am successful. One of our salesmen approached me with the following tale: "Dr. Wear, I took an applicant for $5,000 Retirement Income and had him examined. He said he would take the policy if it were issued standard. He had been issued standard by one company, rated by another and declined by still another within the past year. I should have sent a letter of inquiry to the Home Office before having him examined. I'll be charged for the examination if I don't deliver the policy. It was issued Class D. He is on his way up here. Will you take him on?" I told him I wasn't a salesman. What if I fail? He replied it was no better than he could do. He knew he coudn't deliver the policy. Just at this time the man appeared. The agent introduced me with the remark that I would explain the reasons for the issuance of his policy in a special class. Then he made a hasty retreat and left us alone. I said, "Mr. Stone, Mr. Jones is quite exercised because your policy was issued Class D, which requires an increase of thirty-nine dollars and ninety-five cents in the annual deposit. He is confused, as he tells me you are, because you have been issued at the regular rate, at an increased rate, and declined by different companies within the past year. You were

examined by one of our most experienced doctors and he found a heart murmur which he has classified as a defective valve. These impairments are often confusing to doctors. I know that I have missed them and have not always classified them accurately. The murmur may be very faint at times and missed if there are any extraneous noises. Then the defect does not always remain constant. It may progress from a leak to an obstruction. In which event many companies would reject you and others issue in a much higher class. You are not going to improve. You may get worse. We have issued at an equitable and fair rate. Mr. Jones is in his office. He has your policy." Later the salesman wanted to buy me a box of cigars and a bottle of bonded. He said the man sat down and without a word wrote out a check for the full annual premium. Of course, I did not accept any gift, just told him it was Aetna service.

There is a situation which seems to me more prevalent than ten years ago. Applicants declined or offered a contract in a special class are insistently demanding to know the reasons. When the information has been obtained from the personal physician, even though we have the applicant's consent, the problem must be handled with diplomacy. If we refuse to give any information, it causes antagonism and refusal to accept any contract issued. If the applicant is told, he often has a feeling of resentment toward his doctor. We were at a loss to know how to satisfy the applicant and make him feel happy with his policy until we hit upon the following procedure:

"Mr. Jones, our action is due to your medical history which you authorized Dr. Smith to give us. Dr. Smith, in his excellent report, says your present physical condition is good; however, life insurance companies are not interested only in your present condition, but equally important, in your past history, for we know your life expectancy is based on both factors. We also know if we insure a thousand persons with a history like yours, the loss ratio will be greater than normal. Consequently, if we are to remain solvent and be able to pay our claims promptly, we must charge according to the expected loss ratio, just as a fire insurance company must base its rate upon the type of construction and available fire protection." This explanation seems to satisfy

the applicant and makes him feel kindly toward his doctor, and helps us to deliver the contract.

The examiner is our front line of defense in weeding out the uninsurable as well as giving us the information which makes it possible to properly classify risks when applicants are not eligible at the regular rate. He should be contacted at frequent intervals. We visit the examiners who are making most of our examinations from one to three times a year. We have often been a guest in their homes. It is an ideal time to discuss our problems. The general agent has told me of the improved relationship after such a visit.

When a complaint is received about an examiner, we invite the general agent or the complaining agent to accompany me to the doctor's office for a discussion of the trouble. Sometimes the matter is dropped as not being of sufficient importance. Occasionally we invite the doctor to have lunch with the general agent and myself, when the difficulty is discussed. Then at times we do visit the doctor in his office with the agent or general agent to discuss the grievances. In most instances, the situation is due to some misunderstanding, to unavoidable incidents, or to the indifference of the office secretary. It is remarkable how what appears to be a major issue disappears after a little diplomatic conversation.

I have a feeling that the medical department's duties do not end with underwriting the risk and the selection and supervision of examiners, but can be helpful in training salesmen how to get and keep the examiner's cooperation, and further, to use some of its training in psychology to instruct the salesman how to make the applicant happy with his policy, though issued in a special class.

Possibly you have noticed that I do not use such terms as substandard or rated. There is no such contract as substandard, and all policies are rated according to the mortality of the group. We do not issue at the same rate at age 50 and age 25. Nor do we issue at the same cost to an applicant with a heart defect and one without. In the first instance, age is the impairment; in the second, heart. Each has been issued standard according to the mortality of his group.

If we can get the sales department to delete such terms as

"rated" and "substandard", it will help the salesman to deliver the contract and satisfy the applicant that he has been accorded the same consideration as all others in his class.

Summary:

1. Visit the examiner in his office at frequent intervals. A short visit will indicate whether he is indifferent, incompetent or careless.
2. Arrange to have the new examiner at lunch with the general agent or manager with you present.
3. Getting satisfactory examiners and service requires the co-operation of the medical department, general agent or manager and the agent.
4. Do not allow complaints to accumulate, for trivial grievances become serious if allowed to remain unsettled.
5. Do not overlook the doctor's office secretary. She is often the cause for delay in answering correspondonce and in making appointments difficult. We always have a visit with her and explain the importance of our work.
6. Arrange to have a copy of these Proceedings sent to the examiners.
7. Statistics must be used in our work, but in concentrating on statistics, one may forget that he is dealing with people.
8. Standardization is desirable up to a certain point, but it should not be dominant, for then progress ceases.
9. Let us discontinue using the terms "rated up" and "substandard", and convince the sales department it would be to their advantage to do likewise.
10. Finally, as the science of medicine advances, let us be ever alert to make progress in classifying applicants by subdividing some of our groups, as well as adding new groups so that fewer and fewer applicants shall be denied the blessings of the protection which only life insurance can give.

PRESIDENT LEE — Dr. Wear, I am sure that the medical directors are going to read again your paper with great interest, and it will be used as a guide in the conduct of their affairs in relation to medical examiners.

Of course, these meetings all have to come to a close and we are now going to close this one. Before doing so, however, I want to express my great appreciation for the honor you bestowed upon me a year ago. I could not have done the job I have tried to do without a lot of help. I want first to thank my own office force. The girls there have worked overtime, including week-ends. Dr. Anderson has done a grand job with the special equipment. Dr. Talbot has helped in ways too numerous to mention.

In closing these remarks, I wish to thank the committee I have worked with. Dr. Kirkland, our Secretary, is a giant for work and did a magnificent job. I am very sorry our Treasurer, Dr. Walter Reiter, could not be here. Our Editor, Dr. James R. Gudger, was afflicted with virus pneumonia in Portland and had to go back home. We are sorry he could not be with us. Dr. Dewis, with his great experience in handling lunches and dinners, has been very helpful. I am grateful to each one of the speakers who contributed so generously to our program. On behalf of our members, I extend the sincere thanks of the Association.

Last evening I think I introduced all the new officers. I do not know how many are here. Is Dr. Montgomery here? Will you stand up, please? Is Dr. Willis here?

Now I have the pleasure of turning over the Chair and the Office of President to a very fine gentleman whom you all know. I want to say that his fine Company has contributed greatly to the welfare of this organization and to the institution of life insurance.

Earl Bonnett, personally, aside from the official capacity he occupies with his Company, has been a great worker and has contributed mightily also to the organization. So, with a feeling of confidence and with great pleasure, Earl, I turn this gavel over to you.

PRESIDENT-ELECT EARL C. BONNETT — It is with a great deal of trepidation that I assume the responsibilities that go with the honor of being elected to this office. This trepidation is a great deal greater because I have to follow in the footsteps and the shadow of Linford Lee. He has done a magnificent job. This will be one of the outstanding conventions of this Association.

I deeply appreciate the honors and the responsibilities. I assume

them with the hope and assurance that I will have fine cooperation from all of you, so that we can carry on during our year's work the old idea that each year we are of greater service to our individual companies and our policyholders.

Is there any further business to be brought before the meeting?

UNIDENTIFIED SPEAKER — Mr. Chairman, I move that the unanimous thanks of our Association be extended to all of those who have played such important parts in making this convention the most successful one this organization has ever had. I further move that a vote of thanks be extended to our distinguished Chairman for the excellent program and the brilliant manner in which he has conducted these meetings, and also to his charming wife for the gracious way in which she has endeared herself not only to all the wives of the delegates but to the delegates themselves.

Mr. Chairman, I further move that these motions be incorporated in a suitable set of resolutions to be included in the Transactions of this Association.

PRESIDENT-ELECT BONNETT — Is there a second to that motion?

UNIDENTIFIED SPEAKER — I second it.

PRESIDENT-ELECT BONNETT — The Chair will cast a unanimous ballot and it will be so recorded.

Is there any further business to come before the meeting? If not, the Chair will entertain a motion for adjournment.

So moved, seconded, and the meeting is adjourned.

The following doctors were present at some time during the sessions:

C. G. Abbott
C. B. Ahlefeld
L. A. Alesen
F. R. Anderson
K. W. Anderson
W. N. Anderson

N. J. Barker
C. W. Barnett
C. J. Baumgartner
C. C. Beach
J. R. Beard
E. W. Beckwith
J. E. Bee
R. A. Behrman
M. B. Bender
E. S. Bennett
C. C. Berwick
J. E. Boland
William Bolt
E. C. Bonnett
E. L. Boylen
K. F. Brandon
H. J. Brekke
M. P. Brolsma
H. B. Brown
R. F. Brown

D. A. Campbell
P. E. Carlisle
F. H. Chase
N. B. Cole
R. S. Cosby

Max Davidson
Aniceto Del Rio
H. D. Delamere
E. J. Dewees
E. T. Dewey
E. G. Dewis
T. H. Dickson
F. R. Dieuaide
H. W. Dingman
G. G. Dollinger
A. H. Domm
J. P. Donelan
J. B. Doyle
E. J. Drenick
T. C. Dunlop

T. M. Ebers
R. B. Eusden

J. G. Falconer
R. M. Filson
H. M. Frost

D. S. Garner
E. E. Getman
J. W. Gofman
W. S. Graf
Ghent Graves
G. C. Griffith
W. E. Grubbs
B. G. Gurman

N. W. Haddow Hall
G. W. Halpenny
O. E. Hanes
Frank Harnden
J. H. Hayes
I. C. Heron
N. L. Hoffmann
J. L. Humphreys
J. R. B. Hutchinson

A. S. Irving

C. P. Jensen
A. O. Jimenis
A. E. Johann

E. A. Keenleyside
N. R. Kelley
Milton Kerlan
H. B. Kidd
Richard King
C. T. Kirchmaier
H. B. Kirkland
N. L. Knott
Edward Kuck
Paul Kurzweg, Jr.

David Lee
L. D. Lee
L. H. Lee
J. M. Livingston
G. W. Lougheed
M. L. Lowry
R. W. Lyster

F. M. McChesney
William MacDonald
A. J. McGanity
F. J. McGurl
R. E. McLochlin
C. D. Magee
Reuben Marin
R. F. Maronde
F. A. L. Mathewson
L. K. Meredith
M. D. Mieras

L. C. Miller
M. B. Miller
J. T. Montgomery
R. C. Montgomery
A. R. Moritz
H. J. Moss
C. V. Mulligan

A. J. Oberlander
W. F. H. O'Neill

F. R. Parks
O. H. Peterson
P. E. Pickett
Myron Prinzmetal
D. S. Pulford

Reuben Ratner
C. L. Reeder
H. G. Riche
G. P. Robb
Maurice Rogers
H. B. Rollins
R. C. Roskelley
T. F. Ross

L. P. Schroeder
B. T. D. Schwarz
W. H. Scoins
D. L. Selby
E. F. Sheldon
Eugene Simmons
R. R. Simmons
Mayo Smith
W. A. Smith
F. L. Springer
H. F. Starr

J. C. Talbot
G. F. Tegtmeyer
W. B. Thornton
J. E. Toothaker
Joseph Travenick, Jr.
E. E. Treidel

H. E. Ungerleider

B. W. Vale
Vernon Van Zandt
K. B. Vaughan
A. E. Venables

P. C. Waldo
G. H. Walker
G. K. Wallace
S. L. Warren

J. W. Wear
R. L. Weaver
J. A. Wilhelm
A. A. Willander
E. S. Williams
R. H. Williams
R. L. Willis
A. C. Wilson
W. A. Winn
E. A. Witt
L. S. Ylvisaker
G. C. Young
A. F. Zipf

Also present were:

W. S. Bagby
W. S. Bishop
Waldo Boss
George Brooks
R. H. Brown

A. V. Call
John Cannon
H. E. Carlson
J. W. Carter
John Courtney

R. E. Davis
B. J. Dickerson
R. D. Dotts
Leo Dowling
C. J. Doyle

W. S. Entwistle

Mrs. A. C. Feeley
W. E. Fortmueller

C. S. Gillespie
William Gordy
Arthur Gray
Glen Gregg

Mack Hanson
J. E. Harris

J. R. Hartnett, Jr.
Douglas Higginbotham
R. F. Hodge
Miss Irene Hoffman
David Hunt
Ronald Hurley

E. H. Jackson
C. A. Johnson
F. C. Jones

W. C. Kennedy

W. H. Lane
John Logan

E. M. MacRae
J. V. Malone
T. J. Merrill
L. W. Morgan
Harry Morgan

L. J. Oaks
Henry Oberdick

L. N. Parker
Harry Pflaumer
R. V. Proctor

J. R. Pullman
H. B. Reiter
W. L. Reynolds
J. D. Rockafellow
W. R. Rothaermel

Harry Samm
C. H. Savage
W. S. Shaffer
Stanley Smith
A. J. Spingler
William Stofft
Miss Ruth Stewart
A. H. Strubhar
H. L. Sutton
D. K. Swinnerton

Norman Taylor
E. E. Thomas
C. Alan Tobin

E. M. Urich

C. M. Watt
Bruce Weatherhead
T. A. Wiegand
J. C. Wilberding
H. A. Winters

Total attendance at all sessions, 232.

In Memoriam

Deceased since Sixtieth Annual Meeting

J. V. Bell, M. D.
National Fidelity Life Insurance Company
Died September 29, 1952

Joseph K. P. Hawks, M. D.
State Farm Life Insurance Company
Died June 15, 1952

Ira E. Hoffman, M. D.
Washington National Insurance Company
Died February 11, 1952

Edward P. Leeper, M. D.
The Praetorians
Died February 9, 1952

LIST OF MEMBERS OF THE ASSOCIATION OF LIFE INSURANCE MEDICAL DIRECTORS OF AMERICA

Charles B. Ahlefeld, M. D.	Business Men's, Kansas City, Mo.
George E. Allen, M. D.	National, Montpelier, Vt.
Joseph Altman, M. D.	Companion Life, New York City
Henry H. Amsden, M. D.	United Life and Accident, Concord, N. H.
E. A. Anderson, M. D.	Modern Woodmen, Rock Island, Ill.
Frank R. Anderson, M. D.	Pacific Mutual, Los Angeles, Calif.
Karl W. Anderson, M. D.	Northwestern National, Minneapolis, Minn.
Perry A. Anderson, M. D.	Rockford Life, Rockford, Ill.
Robert L. Anderson, M. D.	Reliance, Pittsburgh, Pa.
Thomas M. Armstrong, M. D.	Philadelphia Life, Philadelphia, Pa.
William B. Aten, M. D.	Security Mutual, Binghamton, N. Y.
Donald R. Auten, M. D.	New York Life, New York City
Bernard Baillargeon, M. D.	Alliance Nationale, Montreal, Canada
G. Holbrook Barber, M. D.	Manhattan, New York City
Norman J. Barker, M. D.	Connecticut General, Hartford, Conn.
Gordon P. Barnett, M. D.	Kansas City Life, Kansas City, Mo.
Charles M. Barrett, M. D.	Western and Southern, Cincinnati, Ohio
Daniel S. Baughman, M. D.	Security Life and Accident, Denver, Colo.
Carroll C. Beach, M. D.	State Mutual, Worcester, Mass.

J. Randolph Beard, M. D.	Mutual Benefit, Newark, N. J.
Edgar W. Beckwith, M. D.	Equitable Life Assurance, New York City
James E. Bee, M. D.	Kansas City Life, Kansas City, Mo.
Roland A. Behrman, M. D.	John Hancock Mutual, Boston, Mass.
Murray F. Bell, M. D.	New York Life, New York City
Maurice B. Bender, M. D.	Guardian, New York City
Robert A. Benson, M. D.	Metropolitan, Ottawa, Canada
Roy W. Benton, M. D.	Northwestern Mutual, Milwaukee, Wis.
C. Coleman Berwick, M. D.	Metropolitan, San Francisco, Calif.
Francis P. Bicknell, M. D.	State Mutual, Worcester, Mass.
J. Rozier Biggs, M. D.	Peoples, Washington, D. C.
B. Cosby Bird, M. D.	Preferred, Montgomery, Ala.
William R. Bishop, M. D.	Provident Life Acc., Chattanooga, Tenn.
John E. Boland, M. D.	Country, Chicago, Ill.
William Bolt, M. D.	New York Life, New York City
John M. Bond, M. D.	Northwestern Mutual, Milwaukee, Wis.
Earl C. Bonnett, M. D.	Metropolitan, New York City
Charles M. Bonzey, Jr., M. D.	United States Life, New York City
M. Theodore Boss, M. D.	Home Friendly, Baltimore, Md.
J. Thornley Bowman, M. D.	London Life, London, Canada
Ernest L. Boylen, M. D.	Standard, Portland, Ore.
William E. Branch, M. D.	Constitution Life, Los Angeles, Calif.
Kenneth F. Brandon, M. D.	Aetna, Hartford, Conn.

David J. Breithaupt, M. D.	Manufacturers, Toronto, Canada
Albert W. Bromer, M. D.	Metropolitan, New York City
C. Frank Brown, M. D.	Southwestern, Dallas, Tex.
Frederick R. Brown, M. D.	New England Mutual, Boston, Mass.
Howard B. Brown, M. D.	Massachusetts Mutual, Springfield, Mass.
Leslie Brown, M. D.	Equitable Life Assurance, New York City
Ronald F. Buchan, M. D.	Prudential, Newark, N. J.
Benjamin F. Byrd, M. D.	National Life & Accident, Nashville, Tenn.
Joseph T. Cabaniss, M. D.	Travelers, Hartford, Conn.
Edward J. Campbell, M. D.	New York Life, New York City
Hugh B. Campbell, M. D.	Phoenix Mutual, Hartford, Conn.
Raymond L. Candage, M. D.	John Hancock Mutual, Boston, Mass.
Paul E. Carlisle, M. D.	Prudential, Los Angeles, Calif.
David W. Carter, Jr., M. D.	Reserve Life, Dallas, Tex.
John P. Chapman, M. D.	Pennsylvania Life, Health & Accident, Philadelphia, Pa.
Paul H. Charlton, M. D.	Midland Mutual, Columbus, Ohio
Edmund D. Chesebro, M. D.	Puritan, Providence, R. I.
Harry E. Christensen, M. D.	Union Mutual, Portland, Me.
Robert B. Cleveland, M. D.	Equitable Life Assurance, New York City
Milton H. Clifford, M. D.	New England Mutual, Boston, Mass.
Harry A. Cochran, Jr., M. D.	Lincoln National, Fort Wayne, Ind.
Norman B. Cole, M. D.	Baltimore Life, Baltimore, Md.

Irwin E. Colgin, M. D.	Texas Life, Waco, Tex.
G. R. Collyer, M. D.	London Life, London, Canada
Harry L. Colombo, M. D.	National Life, Montpelier, Vt.
Frederick R. Congdon, M. D.	Berkshire, Pittsfield, Mass.
J. Lindsay Cook, M. D.	Pilot, Greensboro, N. C.
Neil L. Criss, M. D.	United Benefit, Omaha, Neb.
Howard K. Crutcher, M. D.	United Fidelity, Dallas, Tex.
Khurshed J. J. Cursetji, M. D.	Oriental Government Security Life, Bombay, India
John S. Delahaye, M. D.	Empire Life, Kingston, Canada
Harold D. Delamere, M. D.	Crown, Toronto, Canada
Aniceto Del Rio, M. D.	La Nacional, Mexico City, Mexico
Ernest J. Dewees, M. D.	Provident Mutual, Philadelphia, Pa.
Earle T. Dewey, M. D.	Metropolitan, San Francisco, Calif.
Edwin G. Dewis, M. D.	Prudential, Newark, N. J.
Edward S. Dillon, M. D.	Penn Mutual, Philadelphia, Pa.
Harry W. Dingman, M. D.	Continental Assurance, Chicago, Ill.
Nathaniel P. Doak, M. D.	Great Southern, Houston, Tex.
Albert H. Domm, M. D.	Prudential, Los Angeles, Calif.
James P. Donelan, M. D.	Guarantee Mutual, Omaha, Neb.
Gerald D. Dorman, M. D.	New York Life, New York City
James T. Downs, Jr., M. D.	Fidelity Union, Dallas, Tex.
Raymond L. Dross, M. D.	Prudential, Houston, Tex.

Thomas C. Dunlop, M. D.	Manufacturers, Toronto, Canada
Louis B. Dunn, M. D.	Postal, New York City
William W. Eakin, M. D.	Standard, Montreal, Canada
Lyon H. Earle, Jr., M. D.	Connecticut General, Hartford, Conn.
Theodore M. Ebers, M. D.	Connecticut Mutual, Hartford, Conn.
H. Glenn Ebersole, M. D.	Central Standard, Monmouth, Ill.
Laurence B. Ellis, M. D.	Boston Mutual, Boston, Mass.
Jack A. End, M. D.	Northwestern Mutual, Milwaukee, Wis.
Albert H. Faber, M. D.	New York Life, New York City
J. Gilbert Falconer, M. D.	North American, Toronto, Canada
Raymond K. Farnham, M. D.	Metropolitan, New York City
Haynes H. Fellows, M. D.	Metropolitan, New York City
William S. Fewell, M. D.	Liberty, Greenville, S. C.
Ralph M. Filson, M. D.	Travelers, Hartford, Conn.
Rexford W. Finegan, M. D.	Metropolitan, New York City
Harry E. Flansburg, M. D.	Bankers, Lincoln, Neb.
Philip M. L. Forsberg, M. D.	United Life and Accident, Concord, N. H.
Garth E. Fort, M. D.	National Life & Accident, Nashville, Tenn.
John M. Foster, M. D.	Capitol, Denver, Colo.
Robert L. Fransway, M. D.	Continental Assurance, Chicago, Ill.
Edward M. Freeland, M. D.	New York Life, New York City

Clarence E. Fronk, M. D.	Hawaiian Life, Honolulu, T. H.
Harold M. Frost, M. D.	New England Mutual, Boston, Mass.
F. Irving Ganot, M. D.	Prudential, Newark, N. J.
I. Kenneth Gardner, M. D.	Reliance, Pittsburgh, Pa.
David S. Garner, M. D.	Shenandoah, Roanoke, Va.
J. H. Geddes, M. D.	Northern, London, Canada
John T. Geiger, M. D.	Metropolitan, New York City
John P. Gemmel, M. D.	Monarch, Winnipeg, Canada
William M. Genthner, M. D.	Continental American, Wilmington, Del.
Edson E. Getman, M. D.	New York Life, New York City
Edgar G. Givhan, Jr., M. D.	Protective, Birmingham, Ala.
Otto G. Goldkamp, M. D.	Connecticut General, Hartford, Conn.
Robert A. Goodell, M. D.	Phoenix Mutual, Hartford, Conn.
George Goodkin, M. D.	Equitable Life Assurance, New York City
Harry W. Goos, M. D.	Home, Philadelphia, Pa.
J. Keith Gordon, M. D.	Sun, Montreal, Canada
Charles D. Gossage, M. D.	Confederation, Toronto, Canada
Angus S. Graham, M. D.	London Life, London, Canada
George M. Graham, M. D.	Lincoln National, Fort Wayne, Ind.
Albert E. Gras, M. D.	Prudential, Newark, N. J.
Ghent Graves, M. D.	American General, Houston, Tex.

Marvin L. Graves, M. D.	American General, Houston, Tex.
Harris M. Gray, M. D.	Manufacturers, Toronto, Canada
Floyd M. Green, M. D.	Columbus Mutual, Columbus, Ohio
George E. Greenway, M. D.	Western Life Assurance, Hamilton, Canada
C. J. M. Grisdale, M. D.	Connecticut General, Hartford, Conn.
Frederick O. Gronvold, M. D.	Pioneer Mutual, Fargo, N. D.
Richard S. Gubner, M. D.	Equitable Life Assurance, New York City
James R. Gudger, M. D.	Mutual, New York City
Van W. Gunter, M. D.	Jefferson Standard, Greensboro, N. C.
Milton W. Gwinner, M. D.	Western and Southern, Cincinnati, Ohio
Llewellyn Hall, M. D.	Phoenix Mutual, Hartford, Conn.
F. Tulley Hallam, M. D.	Bankers, Des Moines, Iowa
John H. Halliday, M. D.	Australian Mutual, Sydney Australia
Gerald W. Halpenny, M. D.	Royal, Montreal, Canada
Vincent G. Hammond, M. D.	Security Mutual, Binghamton, N. Y.
Ottis E. Hanes, M. D.	Life Ins. Co. of Ga., Atlanta, Ga.
John A. A. Harcourt, M. D.	Toronto Mutual, Toronto, Canada
Charles P. Hardwicke, M. D.	Western Reserve, Austin, Tex.
Frank Harnden, M. D.	Berkshire, Pittsfield, Mass.
Garland M. Harwood, M. D.	Life Insurance Co. of Virginia, Richmond, Va.
Louis E. Hathaway, Jr., M. D.	Monarch, Springfield, Mass.
Howard L. Hauge, M. D.	New York Life, New York City

Walter C. Hausheer, M. D.	Prudential, Newark, N. J.
Harry M. Hawkins, M. D.	Old Line, Milwaukee, Wis.
Thomas L. Hawkins, M. D.	Western, Helena, Mont.
J. Harry Hayes, M. D.	Union, Little Rock, Ark.
Olin C. Hendrix, M. D.	New England Mutual, Boston, Mass.
Ivan C. Heron, M. D.	West Coast, San Francisco, Calif.
William D. Hickerson, M. D.	Union Central, Cincinnati, Ohio
Eugene V. Higgins, M. D.	North American Reassurance, New York City
Ernest C. Hillman, Jr., M. D.	Mutual Benefit, Newark, N. J.
Daniel W. Hoare, M. D.	Penn Mutual, Philadelphia, Pa.
Joseph C. Horan, M. D.	Metropolitan, New York City
Arnold B. Houston, M. D.	Great-West, Winnipeg, Canada
Edward G. Howe, M. D.	Prudential, Newark, N. J.
Thomas B. Hoxie, M. D.	New York Life, New York City
Henry W. Hudson, M. D.	Loyal Protective, Boston, Mass.
John L. Humphreys, M. D.	Reliance, Pittsburgh, Pa.
James H. Humphries, M. D.	Home, New York City
J. Edward Hunsinger, M. D.	Republic Nat'l, Dallas, Tex.
Benjamin L. Huntington, M. D.	John Hancock Mutual, Boston, Mass.
Samuel W. Hurdle, M. D.	Security Life & Trust, Winston-Salem, N. C.
John J. Hutchinson, M. D.	New York Life, New York City
J. Raymond B. Hutchinson, M. D.	Acacia Mutual, Washington, D. C.

Albert S. Irving, M. D.	Commonwealth, Louisville, Ky.
J. Grant Irving, M. D.	Aetna, Hartford, Conn.
Samuel Jagoda, M. D.	State Reserve, Fort Worth, Tex.
Albert O. Jimenis, M. D.	Metropolitan, New York City
Albert E. Johann, M. D.	Bankers, Des Moines, Iowa
Hubert R. John, M. D.	Maccabees, Detroit, Mich.
Joseph W. Johnson, Jr., M. D.	Interstate Life and Accident, Chattanooga, Tenn.
Alfred Kahn, Jr., M. D.	National Equity, Little Rock, Ark.
Victor L. Karren, M. D.	Home, New York City
Edward A. Keenleyside, M. D.	Prudential, Toronto, Canada
Frank J. Kefferstan, II, M. D.	John Hancock Mutual, Boston, Mass.
Charles H. Kelley, M. D.	Columbian National, Boston, Mass.
Newell R. Kelley, M. D.	Phoenix Mutual, Hartford, Conn.
Herbert B. Kennedy, M. D.	Woodmen of the World, Omaha, Neb.
Harry B. Kidd, M. D.	Metropolitan, Ottawa, Canada
Charles E. Kiessling, M. D.	Prudential, Newark, N. J.
Donald G. Kilgore, M. D.	Republic National, Dallas, Tex.
Carl T. Kirchmaier, M. D.	Life & Casualty, Nashville, Tenn.
Henry B. Kirkland, M. D.	Prudential, Newark, N. J.
Norman L. Knott, M. D.	Prudential, Los Angeles, Calif.
Edward Kuck, M. D.	Union Central, Cincinnati, Ohio

Paul Kurzweg, Jr., M. D.	All American Assurance, Lafayette, La.
Walter C. Lamb, M. D.	Equitable Life Assurance, New York City
Phillips Lambkin, M. D.	Guardian, New York City
Paul H. Langner, Jr., M. D.	Provident Mutual, Philadelphia, Pa.
L. Gordon LaPointe, M. D.	Manhattan Life, New York City
H. Franklyn Laramore, M. D.	Connecticut Mutual, Hartford, Conn.
Albert L. Larson, M. D.	Travelers, Hartford, Conn.
Ivan C. Lawler, M. D.	New York Life, New York City
Linford H. Lee, M. D.	Pacific Mutual, Los Angeles, Calif.
James M. Leffel, M. D.	Empire L. & A., Indianapolis Ind.
Harold R. Leffingwell, M. D.	Paul Revere, Worcester, Mass.
William R. Leute, Jr., M. D.	Penn Mutual, Philadelphia, Pa.
T. Herbert Lewis, M. D.	Western States, Fargo, N. D.
Janus C. Lindner, M. D.	Prudential, Newark, N. J.
Everett H. Lindstrom, M. D.	Western, Helena, Mont.
James A. Livingston, M. D.	Liberty National, Birmingham, Ala.
John M. Livingston, M. D.	Mutual, Waterloo, Canada
Gladstone W. Lougheed, M. D.	Confederation, Toronto, Canada
John F. Lovejoy, M. D.	United Life, Jacksonville, Fla.
Cabot Lull, M. D.	American, Birmingham, Ala.
Gerald J. Lunz, M. D.	Knights of Columbus, New Haven, Conn.

Frank M. McChesney, M. D.	Equitable, Washington, D. C.
William J. McConnell, M. D.	Metropolitan, New York City
George McCreight, M. D.	Bankers, Des Moines, Iowa
Howard M. McCue, Jr., M. D.	Life Insurance Co. of Virginia, Richmond, Va.
William MacDonald, M. D.	Teachers Insurance & Annuity Association, New York City
Arthur J. McGanity, M. D.	Dominion, Waterloo, Canada
J. David McGaughey, III, M. D.	Connecticut General, Hartford, Conn.
Frank J. McGurl, M. D.	Prudential, Houston, Tex.
Thomas J. McGurl, M. D.	Mutual, New York City
Charles D. McKeown, M. D.	Farmers & Bankers, Wichita, Kan.
William G. McLaughry, M. D.	Protected Home Circle, Sharon, Pa.
George McLean, M. D.	Sun, Baltimore, Md.
Lawrence L. McLellan, M. D.	Provident Mutual, Philadelphia, Pa.
Ralph E. McLochlin, M. D.	National Old Line, Little Rock, Ark.
William J. McNamara, M. D.	Equitable Life Assurance, New York City
Charles Maertz, M. D.	Union Central, Cincinnati, Ohio
Charles D. Magee, M. D.	Missouri Insurance Company, St. Louis, Mo.
S. J. Newton Magwood, M. D.	Continental, Toronto, Canada
John Malgieri, M. D.	New York Life, New York City
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National Life & Accident Ins. Co., Nashville, Tenn.	B. F. Byrd, M. D. G. E. Fort, M. D. L. C. Miller, M. D.
National Life Assurance Co. of Canada, Toronto, Canada	E. C. Noble, M. D.
National Life Co., Des Moines, Iowa	L. K. Meredith, M. D.
National Life Insurance Co., Montpelier, Vt.	G. E. Allen, M. D. H. L. Colombo, M. D. A. J. Oberlander, M. D.
National Old Line Insurance Co., Little Rock, Ark.	R. E. McLochlin, M. D.
National Reserve Life Insurance Co., Sioux Falls, S. D.	Rezin Reagan, M. D
New England Mutual Life Ins. Co., Boston, Mass.	F. R. Brown, M. D. M. H. Clifford, M. D. H. M. Frost, M. D. O. C. Hendrix, M. D. R. B. Singer, M. D.

New York Life Insurance Co., New York City	D. R. Auten, M. D. M. F. Bell, M. D. William Bolt, M. D. E. J. Campbell, M. D. G. D. Dorman, M. D. A. H. Faber, M. D. E. M. Freeland, M. D. E. E. Getman, M. D. H. L. Hauge, M. D. T. B. Hoxie, M. D. J. J. Hutchinson, M. D. I. C. Lawler, M. D. John Malgieri, M. D. D. J. O'Leary, M. D. R. W. Pratt, M. D. L. J. Tedesco, M. D.
North American Life Assur. Co., Toronto, Canada	J. G. Falconer, M. D. Eugene Montgomery, M. D.
North American Reassurance Co., New York City	E. V. Higgins, M. D. J. T. Montgomery, M. D.
Northern Life Assurance Co. of Canada, London, Canada	J. H. Geddes, M. D.
Northwestern Mutual Life Ins. Co., Milwaukee, Wis.	R. W. Benton, M. D. J. M. Bond, M. D. J. A. End, M. D. D. F. Rikkers, M. D. G. F. Tegtmeyer, M. D. A. R. Zintek, M. D.
Northwestern National Life Ins. Co., Minneapolis, Minn.	K. W. Anderson, M. D.
Norwich Union Life Insurance Society, Toronto, Canada	W. B. Thornton, M. D.
Occidental Life Ins. Co. of California, Los Angeles, Calif.	E. F. Sheldon, M. D. Joseph Travenick, Jr., M. D.

Ohio National Life Ins. Co., Cincinnati, Ohio	H. H. Shook, M. D.
Ohio State Life Insurance Co., Columbus, Ohio	T. F. Ross, M. D.
Old Line Life Insurance Co. of America, Milwaukee, Wis.	H. M. Hawkins, M. D.
Oriental Government Security Life Assurance Co., Ltd., Bombay, India.	K. J. J. Cursetji, M. D.
Pacific Mutual Life Ins. Co., Los Angeles, Calif.	F. R. Anderson, M. D. L. H. Lee, M. D. J. C. Talbot, M. D.
Pan-American Life Ins. Co., New Orleans, La.	Marion Souchon, M. D. R. C. Voss, M. D.
Paul Revere Life Ins. Co., Worcester, Mass.	H. R. Leffingwell, M. D. J. K. Ruggles, Jr., M. D.
Peninsular Life Insurance Co., Jacksonville, Fla.	E. B. Milam, M. D.
Penn Mutual Life Ins. Co., Philadelphia, Pa.	E. S. Dillon, M. D. D. W. Hoare, M. D. W. R. Leute, Jr., M. D. R. L. Weaver, M. D.
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Wisconsin National Life Insurance Company, Oshkosh, Wis.	E. B. Williams, M. D.
Woodmen of the World Life Insurance Society, Omaha, Neb.	H. B. Kennedy, M. D.

AUTHOR INDEX

Vol. XXXVI—1952

Note—Titles of Original Papers in Plain Type;
of Papers Discussed, in *Italics*

Page

Alesen, Lewis A: Welcoming Address 1

Barnett, Charles W.: Prognosis in Latent Syphilis 107

Bonnett, Earl C.: Remarks 154

Doyle, John B.: The Muscular Atrophies 133

Filson, Ralph M.: The Business of Insurance and the Profession of Medicine 76

Garner, David S.: Greetings from Medical Section, American Life Convention 105

Gofman, John W.: The Present Status of the Problem of Lipid Metabolic Disturbances and Their Relationship to the Genesis of Arterial Disease 13

Griffith, George C.: Problems in Borderline Cardiovascular Disease States 5

Lee, Linford H.: Opening Remarks 1

Mathewson, Francis A. L.: Prolonged P–R Interval in Apparently Healthy People 44

Moritz, Alan R.: Trauma and Heart Disease 100

Prinzmetal, Myron: The Nature and Treatment of the Auricular Arrhythmias 27

Wear, John W.: Observations of a Medical Referee 144

Williams, Robert H.: Syncope, Vertigo, and Dizziness 90

Winn, William A.: Coccidioidomycosis 121

SUBJECT INDEX

Vol. XXXVI—1952

Note—The Names of Authors are printed in Plain Type; of Discussers, in *Italics*

Page

Address, Welcoming. Alesen 1

Business of Insurance and the Profession of Medicine. Filson 76

Coccidioidomycosis. Winn 121

Greetings from Medical Section, American Life Convention. Garner 105

Members of Association:
Active, 159; Companies and Representatives, 179; Deceased since Sixtieth Annual Meeting, 158; Emeritus, 178; Honorary, 178

Muscular Atrophies. Doyle 133

Nature and Treatment of the Auricular Arrhythmias. Prinzmetal .. 27

Observations of a Medical Referee. Wear 144

Present Status of the Problem of Lipid Metabolic Disturbances and Their Relationship to the Genesis of Arterial Disease. Gofman 13

Problems in Borderline Cardiovascular Disease States. Griffith 5

Prognosis in Latent Syphilis. Barnett 107

Prolonged P–R Interval in Apparently Healthy People. Mathewson .. 44

Remarks: Bonnett 154

Lee 1

Syncope, Vertigo, and Dizziness. Williams 90

Trauma and Heart Disease. Moritz 100